ABSTRACTS OF WORLD MEDICINE

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Hygiene and Public Health

1854. **Development and Constitution of the World Health Organization**
Chronicle of the World Health Organization [*Chron. World Hlth Org.*] **1**, 1–43, 1947.

This new publication briefly outlines the growth of international health organizations during the past 50 years. The Pan-American Sanitary Bureau, the International Office of Public Health, the Health Organization of the League of Nations, and the Health Division of Unrra were all bodies which were limited in space, time, and function. To the Brazilian Delegation goes the credit for having insisted that the concept of "health" must be included in the actual Charter of the United Nations. The inclusion of this concept in this basic document represents an acknowledgement that social, economic, and even political progress is conditional on improvement in the state of health of the people. The World Health Organization is the first inter-governmental institution to adopt the term "world" as part of its title. This stresses the fact that disease knows no frontiers and anything less than world action may not only deprive one nation of the benefits of the Organization but may endanger the health of all Member States. The Constitution of the World Health Organization is given in full as an appendix. *G. M. Findlay*

PUBLIC HEALTH

1855. **Effect of Ultra-violet Irradiation of Classrooms on Spread of Measles in Large Rural Central Schools. Preliminary Report**
J. E. PERKINS, A. M. BAHKLE, and H. F. SILVERMAN. *American Journal of Public Health and the Nation's Health* [*Amer. J. publ. Hlth*] **37**, 529–537, May, 1947. 3 figs., 4 refs.

This study was made in three centralized rural schools in which the children came mostly into contact with each other in either the school buildings or the bus. The classrooms had similar ventilating plants and waxed floors; all of the latter were treated with oily anti-dust preparation. The Cato-Meridian school was equipped throughout with ultraviolet lamps and the Port Byron school had half of its classrooms so furnished, while the Mexico school served as a control.

Throughout the investigation the ultraviolet light intensity was maintained at 10 to 20 milliwatts per sq. foot (929 sq. cm.) in upper air and 0·2 to 0·5 milliwatts per sq. foot at face level of standing pupils. The source of light in each classroom consisted of three wall-attached, 30-watt, low-pressure mercury vapour germicidal lamps fitted with reflectors. Despite precautions, several teachers in both schools desquamated and had conjunctivitis. In each case the offending light was detected and adjusted. During an epidemic of measles each case was thoroughly investigated to ascertain the source of infection. Detailed daily records were kept of the ventilation system, indoor and outdoor temperature variations, and relative humidity. Monthly bacteriological examinations were carried out by the open-plate method and the Wells air centrifuge. Since no steps were taken to control the spread of disease in the buses, the latter were considered to be as important in the spread of measles as the classrooms.

In the Cato-Meridian school the outbreak lasted from December to April, while in the control school the outbreak was limited to one of a short, explosive character in March. Port Byron school held a midway position, and further analysis of the cases in this school revealed that in the classes with ultraviolet light the disease was spread over a longer period of time than in the others. The attack rates in the non-irradiated classes among those who used buses and those who did not were 83 and 77% respectively; in the irradiated they were 90 and 69%. Thus the bus played a greater part in the dissemination of measles among the children in the irradiated classrooms than in the non-irradiated. Further investigations are to be made on the effects of ultraviolet irradiation on chickenpox and other infections, and the school buses will be installed with triethylene glycol vaporizers.
A. Michael Critchley

1856. **Effect of Ultraviolet Air Sterilization upon Incidence of Respiratory Infections in a Children's Institution. A Six-year Study**
R. A. HIGGONS and G. M. HYDE. *New York State Journal of Medicine* [*N. Y. St. J. Med.*] **47**, 707–710, April 1, 1947. 5 figs., 12 refs.

In the children's wing of the convalescent branch of St. Luke's Hospital, New York, ultraviolet lamps were hung on the side walls throughout the buildings 7 ft. (2·1 m.) above the floor and so baffled that only the upper half of the room was irradiated. The most effective wave length to kill airborne pathogens has been shown to be 2,537 Å. Such installations produce a ventilation equivalent to at least 100 complete air changes per hour. The authors found no deleterious effects from the light, and the children had no difficulty in sleeping in the faintly illuminated ward. The freshness of the atmosphere aroused comment. When the output of the bulbs diminished the incidence of infection rose. All

bulbs were, therefore, replaced immediately their output fell to 375 microwatts per sq. cm. at 1 ft. (30 cm.). Accumulations of dirt on the bulbs resulted in a rapid decrease in output.

The incidence of institutional respiratory disease from October, 1939, to October, 1942, when there was no ultraviolet air sterilization, was compared with the incidence from October, 1942, to October, 1945, when the ultraviolet lamps were used. The results are shown in a figure. Rectal temperatures were taken morning and evening as a routine. Only children with temperatures over 100° F. (37·8° C.) and showing signs of respiratory infection were included in this study. The incidence of infection during the winter months of the years before the lights were installed was definitely greater than during the later years. During the winters of 1940 to 1941 and 1941 to 1942 there occurred high peaks of epidemic proportions, with a secondary rise in the spring of 1942. The year 1944 to 1945 showed the highest peak for the period with lights; this corresponded with a period during which the incidence of influenza in the general community was very high. During the spring of 1943 the lights were turned off owing to a shortage of bulbs, and the infections increased accordingly. In the control period 4% of children were febrile as against 2·38% in the experimental period. Comparison during the winter months alone shows a difference of 1·96%. These differences are too great to be accounted for by chance or sampling errors. It was noted that among the adult attendants there was less respiratory disease during the period of lights. Experience of contagious diseases was limited, but the authors consider that the lights limited their spread. They conclude that: (1) Contagion due to mouth-to-mouth contact between ambulatory children at play cannot be entirely controlled by ultraviolet air sterilization. (2) The lights effectively inhibit airborne distant spread of infection, thus preventing mass epidemics. (3) The cost of installation and maintenance is justifiable in any institution.

B. S. P. Gurney

1857. **Reaction in Children after Administration of Excessive Doses of "Pentovaccine".** (Реакция у детей после введения чрезмерно больших доз пентовакцины)

V. K. Stefansky, A. Grinfeld, and R. I. Rainerman. Врачебное Дело [*Vrach. Delo*] **26**, 717–718, 1946.

Instead of normal adult serum for measles prophylaxis large doses of "pentovaccine" were given in error to 3 children. This contains the following organisms: *Salmonella typhi*, 1,000 million per ml.; *S. paratyphi A*, 250 million; *S. paratyphi B*, 250 million; *Shigella shigae*, 750 million; and *Sh. flexneri*, 750 million. The organisms are killed by formalin or heat and 0·25% phenol is added. The age of the children ranged from 3 to 4½ years; 2 received 60 ml. and the third 30 ml. subcutaneously. A large swelling developed at the site of the injection (up to 10×12 cm.) and lasted for up to 17 days. In 1 case there was a severe general reaction, but in the other 2 both local and general reactions were very mild. In 2 cases an abscess developed from which sterile pus was aspirated. The mildness of the reaction is attributed to the fact that because the vaccine was used in mistake for human serum it was not shaken in the bottle before the inoculation, so that only a comparatively small number of organisms was injected. The prompt appearance of a local reaction may also have created a barrier to the general absorption of toxins.

D. J. Bauer

1858. **A Survey of Tuberculosis in the Industrial County of Lanarkshire, Scotland**

T. G. Brown. *Journal of Hygiene* [*J. Hyg., Camb.*] **45**, 232–238, May, 1947. 13 refs.

This report is concerned mainly with the evidence regarding relative incidence of bovine and human infection in Lanarkshire. This county, with a population of 506,196, is the most highly industrialized one in Scotland; 443,772 persons reside within the industrial zone, which covers only one-quarter of the total area of the county. The data were collected during the period 1937–42.

Pathological specimens from 311 cases of non-pulmonary and 80 cases of pulmonary tuberculosis were typed. The following table shows the incidence of the two types of tubercle bacillus in these cases:

	Pulmonary Tuber-culosis	Tuberculous Meningitis	Cervical Adenitis	Bone and Joint Tuber-culosis
Human	78 (97·5%)	118 (71·5%)	50 (69·6%)	60 (81·1%)
Bovine	2 (2·5%)	47 (28·5%)	22 (30·4%)	14 (18·9%)

Bovine infections were more numerous in the younger age groups. Of the cases of non-pulmonary tuberculosis, the bovine bacillus was found in 44 of 92 patients under the age of 10, and in only 39 of 126 patients in older age groups. One-half of the cases of tuberculous meningitis occurred in the first 5 years of life or between the ages of 15 and 20. Bovine infections accounted for 28·5% of the total, but the figures for rural and industrial areas were 44·4 and 26·4% respectively. Fifty of the 72 patients with cervical adenitis were under 15 years of age. The figures serve to substantiate observations of regional variation and endorse previous findings indicating a lower proportion of bovine infections in industrial districts.

M. Daniels

1859. **The Influence of Social Factors on the Incidence of Extrapulmonary Tuberculous Infection. An Investigation of the Environment of Tuberculous Patients in Lanarkshire, Scotland**

T. G. Brown. *Journal of Hygiene* [*J. Hyg., Camb.*] **45**, 239–250, May, 1947. 3 refs.

In connexion with the work of isolating and typing tubercle bacilli from 311 Lanarkshire patients (Abstract 1858), the author has collected data relating to social conditions. Of the entire population of the county 32·1% lived in overcrowded conditions. Of the patients studied 72·3% lived in overcrowded houses; the figures

were 55·1% for patients from rural areas and 75·6% for those from industrial areas. The proportion was approximately the same in infections due to the human and bovine bacillus. In the industrial area all of the 25 children under 1 year of age came from overcrowded homes; 20 of the 25 had tuberculous meningitis, 15 of these being due to the human strain of tubercle bacillus. In the industrial area among all patients with meningitis due to the human type of bacillus, 17·2% of those from satisfactory homes and 50·4% of those from overcrowded homes were under 10 years of age; similar figures were found for cases of cervical adenitis.

Analysing the relation of the economic factor to extra-pulmonary tuberculosis, the author found that 44·7% of the industrial group and 20·4% of the rural group came from homes where the family income was not more than ten shillings per head per week. He comments that low economic resources are less important in country districts where food deficiencies are more easily overcome. Of the patients from the industrial area half had a family or personal history of pulmonary tuberculosis.

The author concludes that all the social factors considered were important in determining the incidence of tuberculosis in children and the type of the infecting strain. Substandard housing and a history of contact with open cases of pulmonary tuberculosis were the most important factors in infections with the human strains, and income and milk supply in infections with bovine strains of the tubercle bacillus. *M. Daniels*

1860. ***Salmonella enteritidis* Infection Associated with Use of Anti-rodent " Virus "**

J. G. DATHAN, A. J. MCCALL, J. ORR-EWING, and J. TAYLOR. *Lancet* [*Lancet*] **1**, 711–713, May 24, 1947. 1 fig., 9 refs.

In a household of 5 children and 3 adults a " virus " preparation was used three times for the extermination of mice. About 10 days after it was last employed 4 of the 5 children were found to be infected with *Salmonella enteritidis*. Four case histories are given, the first in full detail with a temperature chart. In this patient, previously a healthy boy, aged 3½ years, the chief feature was a daily swing in temperature from 97° F. to 100° F. (36·1° to 37·8° C.), which lasted continuously for 3 months and recurred occasionally for 7 months. At no time were there any abnormal physical signs, and there was no vomiting or diarrhoea. Blood counts and sedimentation rates showed no significant change throughout the illness, but slight anaemia was early apparent. Laboratory investigations revealed *S. enteritidis* var. *jena* three times in the stools during the first month of the pyrexia but not afterwards. Serum taken in the fourth week agglutinated *S. enteritidis* H to 1 in 125, O to 1 in 125. These titres gradually fell till, during the tenth week, the serum did not agglutinate *S. enteritidis* H but agglutinated O to 1 in 50. Blood culture was sterile. Resistance to other forms of treatment led to the decision to give an immuno-transfusion by immunizing the mother with a vaccine from the *S. enteritidis* strain isolated, bleeding her when her serum showed titres of 1 in 500 H and 1 in 250 O, and giving 300 ml. of blood for the immuno-transfusion. Thereafter the child's condition gradually improved and he recovered completely in 7 months. The authors are doubtful how far the improvement should be attributed to the transference of artificially-induced antibody.

A baby aged 7 months was taken ill at about the same time as the first patient with diarrhoea, which lasted for a week, and blood and mucus in the stools. *S. enteritidis* was isolated from the stools 3 weeks later but was not demonstrable thereafter. There was no pyrexia. The serum was not examined for agglutinins. The faeces and blood of 2 more of the 5 children gave positive results; but the children were almost symptomless.

The authors suggest as alternative explanations for the severity of the illness in the first patient: (1) the persistence of *S. enteritidis* infection outside the alimentary tract; (2) the unstable nature of the child's thermo-regulatory mechanism together with the debility and slight anaemia that followed the initial infection. In support of (1) the authors mention the persistence of a pyrexia of the same type as that exhibited while *S. enteritidis* could still be isolated from the stools in the early days of the infection, and the description by others, of cases of *S. enteritidis* infection of " typhoidal " type. The source of the family infection was traced with reasonable certainty to the boy in the first case, because he had been seen playing with an empty " virus " bottle, and it is recognized that these anti-rodent preparations may be dangerous to man, either directly or as a result of contamination of food by the excreta of vermin infected with the " virus ". The authors state that " there was no indication from the instructions on the bottle that the preparation could be dangerous to man, or that utensils used for the preparation of the bait should not be used for the preparation of human or animal food—an omission which should certainly be remedied ". Of the four main varieties of *S. enteritidis—jena* (human infections), *danysz* (natural rodent infections), *chaco*, (isolated from men during the Chaco war), and *essen* (isolated from man and ducks)—only *jena* and *danysz* have been isolated so far from the commercial anti-rodent " virus " preparations. *Jena* was recovered from the remains of the preparation used in the household and again from the spleen and heart of dead mice after injection each with 0·1 ml. of a 24-hour broth culture of the same remains. *J. Greenwood Wilson*

1861. **A Proposed Test for " Sterilized " Milk**

G. F. V. MORGAN and C. H. CHALMERS. *Nature* [*Nature, Lond.*] **159**, 510, April 12, 1947. 2 refs.

The authors point out that the phosphatase test is not always satisfactory with sterilized milk. This milk may be spoiled by sweet curdling, due usually to atypical forms of *B. cereus* and *B. subtilis*; by an oxidized flavour, associated with large numbers of *B. circulans*; and by a bitter flavour, produced by *B. thermoacidurans*. Sweet curdling is the most common defect and may occur within 3 days of sterilization of the milk. A modified alcohol test is suggested for the detection of defects. The sterilized milk is incubated at 37° C. for 27 hours and then tested with 80% alcohol containing 0·02%

neutral red. Experimentally the authors found that those samples which gave a precipitate developed bitterness or sweet curdling within a period of 3 weeks when held at room temperature—that is, within the period that the milk may be held before sale to the public. If, in addition, there is an acid reaction it is probable that the milk is contaminated with streptococci or with acid-producing sporing aerobes, such as *B. albolactis* and *B. thermoacidurans*. An alkaline reaction rather suggests that the bottles before filling were contaminated with spore-forming organisms. More experiments are necessary to define the exact correlation between the results of the test and the keeping quality of the milk.

W. Savage

1862. **Determination of Filth and Extraneous Matter in Dairy Products**
J. O. CLARKE. *American Journal of Public Health* [*Amer. J. publ. Hlth*] **37**, 728–732, June, 1947.

INDUSTRIAL MEDICINE

1863. **Public Exposure to Lead**
P. DRINKER. *Occupational Medicine* [*Occup. Med.*] **3**, 145–149, Feb., 1947. 10 refs.

Lead poisoning results from absorption of more lead than normal body processes can handle. It is rare among the population at large. Industry does not belittle the toxicity of lead but resents unsubstantiated accusations of lead poisoning. The standard for lead in drinking water is 0·1 parts per million (0·1 mg. per litre), a figure applicable to all beverages. The only standard for foods is the figure set by the U.S. Government for lead in spray residues on fruit, 7·1 parts per million. This is not a severe enough standard for all foods. Daily ingestion of about 0·5 mg. of lead in food or drink with intermittent ingestion of somewhat more is safe; but daily ingestion of more than 0·5 mg. is apt to cause intoxication. Permissible lead dust in U.S. industry is 1·5 mg. per 10 c. metres; the British figure suggested by Legge and Duckering was 5 mg. Ten cubic metres is chosen as the volume of air supposedly breathed in an 8-hour working day. The author suggests that the figure of 1·5 mg. should now be reviewed; it has been applied indiscriminately to all lead dust exposures, and allows for no distinction between the different chemical forms of lead and lead compounds and their known differences in toxicity.

There is a brief review of the literature concerning lead poisoning from painting, from lead petrol, from salvaging scrap, from plumbing, and from welding, and a note on food and drink as a source of lead. *Donald Stewart*

1864. **Exposure to Lead**
R. A. KEHOE. *Occupational Medicine* [*Occup. Med.*] **3**, 156–171, Feb., 1947. 2 figs., 1 ref.

The significance of exposure of the public to lead must be more generally appreciated. Analysis of samples of air breathed in by groups of the population of Cincinnati (not factory workers) showed that in the course of 1 day an individual inhaled about 0·1 mg. of lead. Much of this is finely divided. In controlled experiments on human metabolism over from 6 to 8 months the normal adult was found to excrete a little more lead than he ingested in his food and drink. Although the quantity is small, inhalation of atmospheric lead is so consistent as to form an additional source of lead intake and absorption. Experiments also showed that about 10% of lead, given in solution, is absorbed. This is greater than would be anticipated under ordinary circumstances. Other experimental work indicates that under normal conditions or in incidental lead exposure outside the lead industries the metal does not accumulate in the body, as has been stated frequently in the past. The safe level for the ingestion of lead in food and drink, as determined by the establishment of a level of alimentary lead in normal healthy persons, is greater than 0·3 mg. and less than 0·6 mg. per day.

The normal person has a blood lead concentration between 0·01 and 0·05 mg. per 100 g. whole blood. From 95 to 98% of this is found in the erythrocytes, so that a strong first line of defence is created against intoxication. Increasing severity of exposure to lead in industry is associated with increased lead concentration in blood. Lead excretion in the urine, compatible with complete freedom from the risk of lead poisoning, varies from 0·04 to 0·08 mg. The amount excreted rises to 0·12 mg. without evidence of intoxication. When, in an occupational group, excretion exceeds 0·12 mg. evidence of intoxication is found before long. *Donald Stewart*

1865. **Clinical Significance of Hematologic Changes in Lead Absorption and Lead Poisoning**
W. MACHLE. *Occupational Medicine* [*Occup. Med.*] **3**, 150–155, Feb., 1947. 24 refs.

Lead interferes with synthesis of protoporphyrin and alters the reticular substance of erythrocytes, but there are no specific blood changes in lead absorption. Basophil stippling becomes significant in relation to lead absorption: (*a*) when a uniform method of study is employed for which normal ranges of values have been defined; (*b*) when investigations are repeated frequently on groups and used as an index of trends in exposure; (*c*) as supporting evidence in the diagnosis of lead intoxication; and (*d*) to exclude lead intoxication. Other blood changes—for example in leucocytes and platelets—are more variable and less characteristic than is the stippling. *Donald Stewart*

1866. **Facts and Fallacies Concerning Exposure to Lead**
F. E. WORMSER. *Occupational Medicine* [*Occup. Med.*] **3**, 135–144, Feb., 1947. 16 refs.

As an example of a mistake frequently made the author cites the caption " Lead Fumes Victims " to a newspaper photograph of a group of women lying prone in a factory. The women had been working in a crowded room with closed windows while painting was going on. Investigation showed that no lead paint had been used at the scene of the incident. Even doctors are commonly under the mistaken impression that all paint contains

lead and that anyone exposed to paint is exposed to lead poisoning.

Lead is a common metal, used in the U.S.A. to the extent of 1,000,000 tons annually. It is employed most in the storage battery industry; then in the sheathing of telephone and power cables, the manufacture of paint pigments such as white lead and red lead, and the manufacture of tetraethyl lead for use in petrol, in that order. The risk in these industries is occupational, and preventive measures at the place of work, generally speaking, are good. A summary of current medical knowledge of lead can be found in a recent publication (*Occupational Lead Exposure and Lead Poisoning*, New York, 1943). This publication should be more widely read, as there is still a strong tendency to blame lead for almost any condition that cannot be explained by some other cause. Where suspicions arise it is the policy of the Lead Industries Association to recommend an impartial scientific investigation, full publicity being given to the conclusions. Examples of such inquiries are given. *Donald Stewart*

1867. **The Respiratory Functions of Glass-blowers.** (Dýchací funkce sklářů)
K. KADLEC. *Spisy Lékařské Fakulty Masarykovy University, Brno* [*Publ. Fac. méd. Brno*] **19**, 213–235, 1946. 12 refs.

Eighty glass-blowers employed in the Czechoslovakian glass-blowing trade were examined, clinically, by *x* rays and with the spirometer. The pressure and its duration while glass vessels were being blown were also studied. A decrease in the functional capacity of the lungs becomes apparent after 10 years' employment and is more pronounced after from 20 to 30 years' work. The youngest glass-blower with emphysema was 46 years old and had been at work for 30 years. Emphysema was found in 55% of those working for from 30 to 40 years. There is at present no legislation in Czechoslovakia to provide compensation for this complaint. By more careful selection of recruits those liable to develop emphysema could be excluded. *G. M. Findlay*

1868. **Cadmium Poisoning by Inhalation. Report of a Case**
F. F. HUCK. *Occupational Medicine* [*Occup. Med.*] **3**, 411–414, April, 1947. 4 refs.

Inhalation of industrial cadmium fumes or dust gives rise to a characteristic pulmonary syndrome, whereas ingestion of cadmium causes mainly gastro-intestinal symptoms. Of the former 64 cases have been recorded in the literature since 1858; 10 of these patients died, generally within 10 days. There are few immediate symptoms and the man may continue to work in the fumes, which may be yellowish-brown, for several hours. Within 8 hours the patient complains of irritation of the throat, headache, cough, and chills; 24 to 36 hours later symptoms of pulmonary oedema develop, with shortness of breath, pain in the chest, persistent cough, and weakness. Radiographs show widespread patchy bronchopneumonia or areas of pneumonitis. There is no evidence of a permanent fibrosis of the lung. A further case is described in the present paper. The hazard occurs in the smelting of ores, the making of alloys, vapour lamps, and storage batteries, electroplating, glass colouring, the spraying of pigments, the plating of automobile parts and musical instruments, and welding. *K. M. A. Perry*

1869. **Acute Infections of the Respiratory Tract and Their Control in Industry. With Special Reference to Immunization Against Influenza**
A. M. BAETJER. *Occupational Medicine* [*Occup. Med.*] **3**, 344–360, April, 1947. 48 refs.

Acute respiratory disease is by far the most important cause of sickness absenteeism in industrial workers and is responsible for 40% of all such time lost. All these infections arise from persons who carry the infective agent in the nose and throat; education might therefore be directed to teaching individuals not to spread infection by coughing and sneezing. Industrial undertakings might supply paper handkerchiefs and ask employees to use them, and then to place them in appropriate receptacles. To prevent droplet infection workers should be spaced at least 5 ft. (1·5 m.) apart. Dust-suppressive measures—such as oiling of floors and oil sweeping—are of value and lead particularly to a reduction in streptococcal infections of the respiratory tract. Since ultraviolet irradiation can only be used in the upper air of the room and does not reach the droplets it is of little value in industry. Aerosols also are not very satisfactory, because they are not effective at high temperatures or when humidity is high, their toxicity is not fully worked out, and they do not inactivate organisms in dust or in the larger droplets. Proper sanitation in the preparation and serving of food is important.

Methods for controlling the susceptibility of individuals to respiratory infections include immunization by vaccination. Influenza virus A and B vaccine will greatly reduce the incidence of these diseases during the period of an epidemic. The duration of the immunity has not yet been determined, and since epidemics cannot be accurately forecast it would seem better not to urge vaccination in anticipation of an epidemic, even though it might slightly reduce the annual rate of disease. The continuous administration of sulphadiazine for prophylactic purposes is dangerous, because it may lead to development of drug-resistant strains of organisms. Experiments have shown that neither irradiation of workers with ultraviolet light nor the addition of vitamins to their ordinary diet will increase their resistance to infections of the respiratory tract. Protection against chilling of the body is important, since chilling, inclement weather, or a considerable fall in outdoor temperature lowers the resistance of some persons to infections of the respiratory tract. *K. M. A. Perry*

1870. **On Occupational Diseases of the Skin among Paint Factory Workers, Painters, Polishers and Varnishers in Finland.** [In English]
V. PIRILÄ. *Acta Dermato-venereologica* [*Acta derm.-venereol., Stockh.*] **27**, Suppl. 16, 1–163, 1947. 14 figs., Bibliography.

1871. **Industrial Pathology in Varnishers. Note I.—Clinical Observations.** (Sulla patologia professionale dei verniciatori. Nota I.—Osservazioni cliniche)
S. SESSA and F. M. TROISI. *Folia Medica* [*Folia med., Napoli*] **30**, 129–138, 1947. 21 refs.

The authors classify the substances used in the application of varnishes, which are usually projected from a spray-gun. These are the cellulose ethers, the solvents and diluents, the resins which give brilliance, and the pigments. This method of application is both rapid and cheap, but the concentration of the vapours to which operatives are exposed may reach a dangerous level. When harmful effects are noted it is difficult to attribute them unequivocally to any one constituent of the varnishes, since these are complex mixtures. Absorption occurs through the lungs and the digestive tract, and a few of the substances may penetrate the skin.

Symptoms fairly often seen include abdominal pain and cramps, nausea, and periods of anorexia. Headache and vertigo are occasional complaints with confusion and weakness. Urobilinuria is common and in some workers remains more or less permanent. Mixtures of benzine and of benzene and its homologues, aniline and its derivatives, and lead compounds may be used and cause blood changes which, since several substances may be employed at once, cannot always be attributed to any one factor.

The authors investigated the conditions in a shop employing 20 workers. The most frequent complaints were of gastritis, pharyngitis, headache, and weakness. Fifteen patients were anaemic. All the employees were women and 12 had menstrual disturbances. The liver was enlarged in 7 cases. Symptoms were more common in those who had worked 5 years or more. During the war most of the work had to be done with a brush or a rag and only recently had spray-guns been used again and a proper system of exhaust ventilation been installed.

It was thought that acetone accounted for many of the symptoms, for it comprised more than half of the mixtures used. Butyl and ethyl acetate were present in smaller quantity. As a narcotic substance acetone has an affinity for lipids and is thus likely to damage the nervous system. Persons suffering from chronic acetone poisoning lose weight, become anaemic, and have urobilinuria. In experimental animals degenerative changes in the liver, kidneys, and suprarenals have been noted. The aliphatic esters of acetic acid irritate mucous membranes and the air passages more than acetone but are less narcotic in their action. It is concluded that in the group investigated most of the symptoms were due to acetone and the acetic acid compounds.

G. C. Pether

1872. **Vaccination of Industrial Workers Against Smallpox**
L. C. MCGEE. *Occupational Medicine* [*Occup. Med.*] **3**, 406–410, April, 1947. 13 refs.

Avoidance of epidemics was of paramount importance between 1942 and 1945, and therefore 50,245 workers in several plants were vaccinated against smallpox. Because of reaction to the vaccine 641 (1·2%) lost time from work. The average worker so affected lost 2·43 days, males and females showing no difference in frequency, severity, and disability rates for illness from this vaccination. The needle point was pressed tangentially on to the skin of the arm ten to thirty times in such a manner that the point broke the horny layer in an area some 3 mm. in diameter; the lymph was then allowed to dry on this area. There were no cases of encephalitis, myelitis, tetanus, generalized vaccinia, eczema, or other widespread skin diseases. Malaise, low-grade fever, pain, swelling, and redness of the arm at the site of vaccination accounted for most of the absences from work. Cellulitis of the arm with axillary adenopathy occasionally caused an absence of more than 3 days. Workers over 60 years of age who had not previously been vaccinated had an appreciably higher disability rate than did the young workers. In one factory 7 out of 54 such men lost a total of 21 days from work because of reactions.

K. M. A. Perry

1873. **Herpes Zoster Appearing after Trauma**
J. V. KLAUDER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **134**, 245–248, May 17, 1947. 27 refs.

After a review of the literature on herpes zoster following trauma, 8 cases are briefly described. The affected area was the face in 5 cases (with corneal involvement in 2), the chest in 2, and the arm in the remaining 1. In 3 cases there was slight trauma to the skin without laceration; in 1 slight laceration had occurred; 2 followed injury to an eye, and one removal of a wart by electrodesiccation. The interval between trauma and appearance of herpes zoster was 1 day in 1 case, 3 days in 3 cases and 2, 7, 9 and 14 days respectively in the remaining cases. The possibility that the trauma activated a latent virus is discussed. The incubation period of spontaneous herpes zoster is not known; from experimental evidence and clinical observations (herpes zoster occurring after exposure to chicken pox) the incubation period seems to vary between a few days and about a fortnight. From the author's observations and the literature on herpes zoster after trauma it is concluded that if herpes zoster appears at an interval of from 1 day to 3 weeks after an injury and at the site of the injury, the trauma may reasonably be considered as an aetiological factor. This relation is of importance from the point of view of the Workmen's Compensation Act.

A. Schott

1874. **Social and Occupational Factors in the Aetiology of Skin Cancer**
J. A. RYLE and W. T. RUSSELL. *British Medical Journal* [*Brit. med. J.*] **1**, 873–877, June 21, 1947. 7 refs.

This article can best be summed up by quoting in full the authors' summary and conclusions.

"The annual number of deaths from cancer of the skin, excluding that of the penis and scrotum, is approximately 1,000 per annum in England and Wales, and the mortality in males is about 70% in excess of that in females.

The mortality for both males and females from cutaneous cancer is much greater in Ireland than in England and Wales, whereas the Scottish male experience is decidedly more favourable. The face is the principal site involved. The ear is next in frequency. The mortality has a definite gradient with social grouping for the wives of workers, but for the males it would seem to have both a social and an occupational relationship, and the latter is seemingly the more important. These findings, and the anatomical character of some of the sites affected, suggest, on the one hand, that atmospheric soot or grime (as in the case of scrotal cancer) may need to be considered as an aetiological factor. On the other hand, ultra-violet radiation from the sun may be responsible for skin cancers in exposed sites. Heat, or heat plus grime, may be operative in such occupations as that of furnace-men, if face and hands should be shown to be frequently involved in these workers. Classification according to site in official returns is needed to increase the value of correlations with occupational or other social factors. Correlation with geography, or hours of sunlight in different parts of the British Isles and elsewhere, should also have value." *E. C. B. Butler*

1875. **Problems of Shallow Water Diving. Report Based on Experiences of Operational Swimmers of the Offices of Strategic Services**
C. J. LAMBERTSEN. *Occupational Medicine* [*Occup. Med.*] 3, 230–245, March, 1947. 1 fig., 10 refs.

The author describes an oxygen rebreathing apparatus which was developed during the war of 1939–45 for the use of free underwater swimmers to enable them to enter enemy harbours and attach explosive charges to the hulls of ships and to carry out underwater reconnaissance. The apparatus can also be used for mine rescue and fire fighting. In the underwater environment the diver is exposed to problems associated with great pressures. The first of these is otitic barotrauma. Pinching of the nostrils and a mild expiratory force will normally blow air through the Eustachian tubes and equalize the pressure on the two sides of the tympanic membrane; if this is not achieved pain will be felt in the unequalized ear at a depth of 15 ft. (4·6 m.). If this pain is ignored rupture of the membrane may result, and may be associated with the rupture of congested blood vessels. For the same reasons there may be severe pain in the air sinuses and similar haemorrhage may occur. For each 33 ft. (9·9 m.) of descent into the sea there is an increase of 1 atmosphere in the partial pressure exerted by the pure oxygen and at high partial pressures the gas becomes toxic. At 66 ft. a sensation of generalized nervous excitability develops after about 30 minutes. There is a sense of impending danger and trembling of the hands, with increasing abruptness of inspiration, which, in a few minutes, becomes a series of staccato jerks. This respiratory convulsion may progress to spasm of respiratory muscles, which opposes both inspiration and expiration. Dyspnoea becomes severe and vision blurred, and twitching of the face results. The mind, however, remains clear to the end. The symptoms occur more slowly at less depth and are relieved immediately the diver ascends. If a beginner holds his breath in ascent, thus preventing the escape of expanding air, a lung may be ruptured. Caisson disease or the " bends " cannot arise as a result of diving with an oxygen rebreathing apparatus because pure oxygen and not air is inhaled; the small amount of nitrogen present in the respired gas is not sufficient to cause this condition. Likewise the absence of hose to the surface and the presence of a safety valve on the mask mean that the phenomenon of " squeeze " cannot occur.

In tropical waters injuries may result from underwater creatures, such as coral, jelly-fish, sea-urchins, sharks, barracuda, moray eels, rays, and octopus. All these are described. In temperate waters the low temperatures place a limit on the capacity of the diver to work. The naked diver becomes exhausted after 15 minutes at 55° F. (12·7° C.), 45 minutes at 60° F. (15·6° C.), and 2½ hours at 70° F. (21·1° C.). Clothing may be used to prolong the time but it may make swimming impossible. Daily diving predisposes to otitis externa. Occasionally the wearing of a face mask in strange waters at night may bring out latent tendencies to claustrophobia.

When the apparatus is used for fire fighting or mine rescue the increased carbon dioxide from muscular exertion may give rise to symptoms if the worker neglects to refill the canister with soda lime with each change of oxygen cylinder. The dust from either the soda lime or the " baralyme " may be inhaled, and this may result in a mild chemical irritation of the pulmonary passages if the dust is not sifted or blown from the absorbent before it is put in the canister.

Asphyxia can result from excess of nitrogen in the breathing apparatus if the oxygen supply fails. This is not associated with distress; a sensation of well-being occurs, with, later, mental confusion, which prevents the worker from overcoming his difficulty. Unconsciousness and death may follow. This can be prevented if the breathing bag and lungs are cleared of air before the circuit is closed to breathe oxygen. The absence of excess nitrogen then makes this form of asphyxia impossible. *K. M. A. Perry*

1876. **Some Anatomical Problems in Naval Warfare**
G. WEDDELL and H. D. DARCUS. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] 4, 77–83, April, 1947. 5 figs., 2 refs.

In general these problems are concerned with the determination of conditions of work which allow personnel to perform certain routine operations to the best advantage, the results of such findings then being applied to the design of machines or weapons so far as mechanical requirements and considerations of limitation of space and weight permit. Two examples have been chosen to illustrate the application of the principles employed—seats and high-angle optical sights—both made more necessary by the increasing menace from air attack in modern naval warfare.

The chief requirements of an " ideal " seat for use in naval operations are: (1) The accommodation of individuals of different body dimensions within the 90% range—that is to say, the seat must accommodate 90%

of all naval personnel without the operator fouling surrounding structures. A simple single adjustment of seat height must be provided, and the adjustment of seat level must be related to the foot-rest and also to the oculars of the sight. (2) The ability to attain the maximum degree of body stabilization to counteract movement of the ship and the guns. Body stabilization by the use of a retaining mechanism is undesirable and should be effected by the operator himself, with a minimum muscular effort, by counter-pressure between a foot-rest and back-rest. (3) The elimination of fatigue. The seat must provide an efficient comfortable support to the body over prolonged periods; to achieve this, attention must be paid to the design of the seat cushion, foot-rest, and back-rest. (4) Freedom from breakdown. The seat assemblage must be capable of withstanding very severe usage and the construction of the seat must combine maximum strength with minimum weight and size.

Calculations for dimensions of the seat were based on the American Fort Knox survey of body measurements of military personnel. The optimum position of the foot-rest and back-rest in relation to the seat to obtain maximum pressure was calculated from the result of direct experiment by Hugh-Jones on thrusts exertable on tank brake- and clutch-pedals. Consideration was also given to the size and slope of the cushion, its correct resilience, the position of the back-rest in relation to the back of the seat, the efficiency and comfort of the support given, the position of the foot-rest in relation to the seat, and to fitting lateral thigh supports to the sides of the seat.

In the case of high optical sights two important factors need consideration. The position of the operator must be such that his eyes are related correctly to the binocular eyepieces, both in the vertical and the horizontal plane. This necessitates the design of a seat which allows essential adjustment to be made with ease and rapidity. Also the binocular movement must be such that it follows the natural track taken by the eyes during elevation. Practical tests showed that the vertical adjustments of the eyes to the eyepieces is of extreme importance; the optical axes of the eyes of the observer and of the binoculars must be coincident. The average eye height of the seated subject was found to be between 30 and 34 in. (75–85 cm.). To allow for observers of varying stature the seat used must be adjustable through the required range. It was found by experiment that the natural position of the eyes in 50 individuals varied from 4½ to 6 in. (11·25–15 cm.) in front of the vertical plane through the back-rest. Subsequent trials showed that, providing the position of the eyepieces did not vary by more than 1 in. (2·5 cm.) on either side of the average, there was insufficient justification for a special adjusting mechanism in the sight.

The method used to determine the natural track of the eyes was an extension of that previously adopted by the Admiralty Research Laboratory at Teddington. The mean track of the eyes was arrived at by the comparison of cinematograph films of the act of sighting. The track of the eyes is found to describe two major curves with different centres: the first, described by the eye from 20 degrees depression to about 40 degrees elevation, corresponds to the combination of head and neck movements; the second, described by the eyes above 40 degrees elevation, is chiefly due to movements of the trunk. The oculars can be made to travel approximately along the track of the eyes by pivoting the sight at the centre of the mean of the two curves; or, more accurately, if a movable pivot is incorporated so that the binocular eyepieces actually follow the mean track of the eyes described from 20 degrees depression to zenith. When both methods were put to the test in 100 unselected subjects, the second, incorporating the movable pivot, resulted in 90 of the subjects sighting at 90 degrees of elevation without strain. *A. J. Amor*

1877. **Loose Versus Close-fitting Clothing for Work in "Tropical Heat"**

C. P. YAGLOU and M. N. RAO. *Journal of Industrial Hygiene and Toxicology* [*J. industr. Hyg.*] **29**, 140–142, March, 1947.

In order to ascertain the effects of various kinds of clothing designed for work in warm and humid atmospheres 3 men wearing the clothes to be tested performed mechanical work in an air-conditioned room at 85° F. (29·4° C.), and with a relative humidity of 85%. The air movement, as recorded by a thermo-anemometer attached to the working subjects, was 70 feet (21 m.) per minute. The men stepped up and down a two-step platform 8 times a minute, and this required a total body energy expenditure of 255 cal. per hour. All the subjects preferred to work unclothed, and they then secreted an average of 521 g. of sweat in 2 hours. When wearing loose-fitting pyjamas weighing 320 g. they secreted 610 g. of sweat, and with a close-fitting cotton union suit (480 g.) they secreted 694 g. When wearing a two-piece jungle suit consisting of 5 oz. (141·7 g.) of densely woven poplin and heavy boots (weighing 950 g. altogether), they secreted 756 g. of sweat when the trouser legs and jacket collar were open, and 984 g. when they were closed. The closed jungle suit and the close-fitting cotton suit were particularly disliked because they became damp and sticky. The rise in body temperature and pulse rate were but little affected by clothing, but the rate of sweat secretion closely followed the degree of heat discomfort experienced. *H. M. Vernon*

1878. **Effects of Climatic Extremes**

M. CRITCHLEY. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **4**, 164–190, July, 1947. 54 refs.

1879. **Dust and its Control as a Means of Disinfection of Air**

C. G. LOOSLI. *American Journal of Public Health and the Nation's Health* [*Amer. J. publ. Hlth*] **37**, 353–359, April, 1947. 40 refs.

1880. **Industrial Eye Surgery and Treatment**

L. C. POTTER. *Industrial Medicine* [*Industr. Med.*] **16**, 350–352, July, 1947. 1 fig.

For Industrial Toxicology, see Abstracts 1959–1960.

Anatomy and Cytology

1881. **A Rapid Supra-vital Staining Method for Assessing the Viability of Human Spermatozoa**
A. C. CROOKE and A. M. MANDL. *Nature* [*Nature, Lond.*] **159**, 749, May 31, 1947. 1 ref.

The authors describe a method of assessing viability of human spermatozoa, based on that to be published by Emmens. Four or 5 drops of seminal fluid are well mixed with 1 drop of the supravital stain (50 ml. distilled water; 1 g. "revector soluble blue 706"; 1·5 g. glucose; 0·1 g. sodium chloride; 0·3 g. disodium hydrogen phosphate, hydrated; 0·005 g. potassium dihydrogen phosphate, anhydrous; the solution must be freshly prepared or made up in 1 ml. ampoules and autoclaved). The mixture is left for 2 to 3 minutes. The spermatozoa remain motile in this stain as long as they do in seminal fluid. A smear made from one drop of the mixture is dried in air and fixed in alcoholic mercuric chloride (half volume of saturated $HgCl_2$ in distilled water + half volume of absolute alcohol) for 15 to 20 seconds, dipped into alcoholic iodine (90% alcohol containing enough iodine in potassium iodide to make a straw-coloured solution) and then into 90% alcohol and allowed to dry. It is counterstained with 1% neutral red in distilled water for 15 to 30 seconds and differentiated carefully in 90% alcohol. The smear may then be examined directly by oil immersion or passed through absolute alcohol and mounted in Canada balsam.

The nuclei of dead spermatozoa stain blue or purple, while those of living spermatozoa are clear red.

Peter C. Williams

1882. **Development of Bone Marrow in Adult Animals**
B. STEINBERG and V. HUFFORD. *Archives of Pathology* [*Arch. Path.*] **43**, 117–126, Feb., 1947. 7 figs., 8 refs.

An experimental study was made of the regeneration of bone marrow after its complete extirpation from the tibia of rabbits aged 8 to 10 months. Removal of the marrow from the tubular shaft of the bone was achieved in the following manner. A small hole was drilled at one end of the shaft and a larger hole at the other end. Into the smaller opening a tightly fitting silver cannula was placed through which sterile liquid paraffin was forced from a syringe. The marrow was thus completely extruded through the larger aperture. The holes were then sealed by bone wax. Sixty tibiae in 44 rabbits were prepared in this way. The animals were later killed after 1 to 60 days, and sections were made at different levels of the bone and the progress of regeneration was studied in this way. Differential cell counts were also made on the regenerating marrow on the control side (where only one tibia was operated upon), and on the marrow extruded at the beginning of the experiment. [Only a summary in diagrammatic form of the data so collected is recorded. It is a pity that no protocols are given in the report of a considerable experiment of this type, where tissue reactions in individual animals might vary widely. None the less the results, summarized below, are of much interest.]

Within the first 9 days the tibial endosteum throws out sheets of primitive reticulum cells and bone trabeculae. Vacuolation and coalescence of the reticulum cells form fat spaces, and capillaries accompany the new tissue growth. Between the twelfth and seventeenth days islands of haemocytoblasts, myeloblasts, and erythroblasts are seen near the margins of and in between the fat spaces, and by the twenty-first day the marrow cavity becomes filled and the newly-formed bone trabeculae begin to disappear. There is, however, no uniformity in the degree of myeloid cellularity. In 30 days myeloid cells, and particularly erythroblasts, are much more numerous. Megakaryocytes are seen shortly afterwards in numbers approaching their normal distribution. From the fiftieth day erythroblastic elements are hyperplastic, other myeloid cells being usually present in smaller numbers than normal, but some islands of primitive reticulum cells and partly formed fat spaces still remain. The regeneration of marrow in these adult animals followed closely the pattern of foetal development. The presence of fat spaces in the marrow was thought to be a prerequisite for the growth of myeloid elements. Sealing off the epiphyseal ends of the bone tended to retard but not to prevent myeloid transformation.

Douglas H. Collins

1883. **Revision of the Venous System: The Role of the Vertebral Veins**
W. F. HERLIHY. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 661–672, May 31, 1947. 8 figs., 22 refs.

The author presents a critical review of current concepts of the morphology of the venous system and offers a new hypothesis in which the vertebral plexus assumes much greater importance than has hitherto been ascribed to it. He promises experimental evidence in support of his views in a further paper.

The following common assumptions are rejected: (1) that all blood returns to the heart from the upper part of the body by way of the superior vena cava and from the lower part by way of the inferior vena cava; (2) that all blood contained in the veins is in active circulation. It has been long believed that some of the blood leaves the brain by way of emissary veins, while thrombosis of the superior vena cava or ligation of the internal jugular is not incompatible with life. Blood can drain from the base of the brain into the vertebral plexus, and reach the heart by routes other than the vena cava. Batson showed that a radio-opaque fluid injected into the dorsal vein of the penis passes by way of the prostatic plexus partly into the vertebral plexus through the veins of the sacral body and wings of the

ilia. The vertebral plexus thus provides a pathway up and down the spine, linking the caval systems, but not involving the heart or lungs directly. The extent and connexions of this plexus are not revealed in formalin-hardened subjects. The mass of thin-walled veins, when dilated, covers the whole surface of the vertebral canal, and anastomoses freely with the veins of the brain, meninges, spinal cord, bones of the skull, bodies of the vertebrae, and so forth. Communications exist with the veins of the pelvic viscera and the left renal and supra-renal veins. The veins of the vertebral plexus are peculiar in that the diameter lessens as they approach points of junction; they are most dilated where they are devoid of anastomotic connexions. Thus they are well adapted to form an extensive reservoir, the capacity of which is probably never less and usually much more than 200 ml.

This system of veins contains a reserve of blood, serves as a mechanical buffer, and regulates the cerebro-spinal-fluid (C.S.F.) pressure. The author believes that variation in the capacity of the plexus is the main factor producing change in C.S.F. pressure. The almost instantaneous rise in pressure during the Queckenstedt test is compatible with the view that blood is diverted from the jugular system to the vertebral plexus, dilatation of which within the rigid spinal canal causes the pressure change. Any rise in intrathoracic or intra-abdominal pressure, as on coughing, produces a rise in the arterial pressure. The important arteries of the central nervous system are protected against rupture by the associated rise in C.S.F. pressure, itself the result of the expulsion of blood from the veins of the body wall and viscera into the vertebral plexus. Dilatation of the veins of this plexus reduces the volume of the subarachnoid space. The surging movement of blood into and out of the vertebral plexus is responsible for the circulation of the C.S.F. The plexus has important pathological implications, presenting a route by which malignant growths and other pathological processes may spread from the pelvis to the spine and brain.

The pattern of the venous system differs fundamentally from that of the arteries, which follow a radial pattern, with some peripheral but no central anastomoses. The veins are arranged in five concentric, mutually anastomosing, strata: (1) veins of the central nervous system; (2) epidural veins; (3) veins of the axial skeleton; (4) veins of the active stratum (soft tissues below the deep fascia and muscles); (5) subcutaneous veins. Veins in each stratum are arranged in networks parallel with the surface of the body; arteries run singly and perpendicular to the surface. All the great veins are found in the fourth stratum. The primitive plexiform arrangement of this stratum has been modified by the development of the body cavities and by the need for a direct venous return to the heart in order to maintain the circulation. It is the active stratum which provides this venous return; the other strata play a much more passive part. The two chief elements of the venous system are therefore: (*a*) the caval system concerned with the maintenance of the circulation, and (*b*) the vertebral system concerned with the adjustment of venous and C.S.F. pressure. *H. Hughes*

NERVOUS SYSTEM

1884. **Anatomy of the Thoracic Sympathetic Trunk in the Newborn and in Foetuses.** (Über die Anatomie des Truncus sympathicus thoracicus bei Neugeborenen und Feten)

E. K. NÄÄTÄNEN. *Acta Societatis Medicorum Fennicae "Duodecim" [Acta Soc. Med. "Duodecim"]* **23**, 15–27, 1947. 3 figs., 3 refs.

The anatomy of the thoracic sympathetic trunk was investigated in 50 foetuses and newborn infants. The results were compared with those of Matsui (*Acta schol. med. Kioto*, 1925, **8**, 1) on Japanese foetuses. The narrowing of the sympathetic cord usually observed in Japanese foetuses was seen in only 41% of the Finnish cases. There were discontinuities of the cord in 32·6% of Matsui's cases but in only 11% of the author's material. In no case was there more than one discontinuity. The number of ganglia was between nine and thirteen, and was most commonly eleven. The last cervical and the first thoracic ganglia were completely united in 35% of cases, and quite distinct in 51%. The first two thoracic ganglia were also frequently united or very close together. A stellar ganglion, formed by the junction of the last cervical and first two thoracic ganglia, was found in 28% of Finnish cases as compared with 21·7% of Japanese. Unions between two or more lower ganglia were not uncommon. The first thoracic ganglion was usually the largest and the size of the ganglia decreased down to about the ninth. The positions of the ganglia were very variable. As a rule they lay in or cranial to their corresponding intercostal spaces. The lowest ganglia often lay on the surface of a vertebra. *R. Barer*

1885. **Contributions to the Anatomy of the Splanchnic Nerves.** (Beiträge zur Kenntnis der Anatomie der Nervi splanchnici)

E. K. NÄÄTÄNEN. *Acta Societatis Medicorum Fennicae "Duodecim" [Acta Soc. Med. "Duodecim"]* **23**, 1–14, 1947. 1 fig., 6 refs.

The origin of the splanchnic nerves was determined in 50 foetuses and newborn infants. The greater splanchnic nerve arose between the third and eleventh thoracic ganglia by 2 to 5 roots. The eighth and ninth ganglia contributed roots most frequently. A splanchnic ganglion (Arnold) was found in 15 cases. In 3 of these it was found on both sides, in 8 only on the right, and in 4 only on the left. It was generally oval, 4·3 mm. long by 3 mm. broad, and was most commonly situated at, or slightly below, the junction between the most caudal root and the main trunk. The lesser splanchnic nerve usually arose by one or two roots from the region of the eighth to the twelfth ganglia. The tenth or eleventh contributed fibres most frequently. The nerve was absent on both sides in 1 case, on the right in 2 cases, and on the left in 2 cases. The least splanchnic nerve was seldom found, and then usually only on one side. It generally arose by one root from the eleventh or twelfth ganglion. *R. Barer*

Physiology and Biochemistry

1886. **Glucose Exchanges and Cerebrospinal Glucose Content.** (Il ricambio glucidico e la glicorrachia)
V. GIUNTI. *Minerva Medica* [*Minerva med., Torino*] **2**, 309–310, Oct. 13, 1946. 1 fig., 1 ref.

Having previously found that the injection of glucose into the cerebrospinal fluid leads to hypoglycaemia, the author now shows that the oral administration of 0·9 g. glucose per kilo body weight in 5 dogs led to a rise in glucose content of the cerebrospinal fluid, which preceded by 15 to 25 minutes the descent of the blood-sugar curve. These facts are in accord with the idea that the sugar-regulating centres producing hypoglycaemia are stimulated by a rise in glucose concentration in the cerebrospinal fluid. *T. R. Parsons*

1887. **Physiologic Condition of the Heart in the Natives of High Altitudes**
A. ROTTA. *American Heart Journal* [*Amer. Heart J.*] **33**, 669–676, May, 1947. 32 refs.

Natives living 4,540 metres above sea level were studied. In 69·5% of 400 subjects there was an average increase of 19·5% in the transverse diameter of the heart. The various degrees of right axis deviation were found in 59%, and tracings typical of cor pulmonale were common. The systolic blood pressure tended to be low, with a normal diastolic pressure and a reduced pulse pressure. Venous pressure was higher than at sea level. Reduplication of the second sound, confirmed by a phonocardiogram, was commonest where there were signs of right ventricular preponderance. It was concluded that at high altitudes the heart is working almost at its maximum capacity, and a very long stay in high altitudes is likely to be harmful from a cardiac point of view. *James W. Brown*

NUTRITION

1888. **Gynecomastia due to Malnutrition. I. Clinical Studies**
G. KLATSKIN, W. T. SALTER, and F. D. HUMM. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **213**, 19–30, Jan., 1947. 2 figs., 52 refs.

Forty-eight of about 300 men released from Japanese prison camps had or had had definite gynaecomastia with a tumour mass in one or both breasts. During their term of captivity they were seriously undernourished. The condition developed after prolonged malnutrition or, in about a third of the cases, shortly after a normal diet was resumed. In spite of this initiation or exacerbation of the gynaecomastia when normal feeding was started the continued normal diet cured the condition after several months. The prison diet was deficient in protein, calories, and vitamins; large doses of vitamin-B complex did not improve the recovery rate. Twenty of the patients had liver enlargement or impaired liver function. Only 25 had a history of acute infective hepatitis. The impairment of testicular function and loss of libido common among the prisoners could not be correlated with the incidence of gynaecomastia. It is concluded that the condition was due to the malnutrition—perhaps by liver damage interfering with oestrogen inactivation or by loss of androgenic function by lowered testicular or pituitary activity. [See Abstract 1889.]
Peter C. Williams

1889. **Gynecomastia due to Malnutrition. II. Endocrine Studies**
W. T. SALTER, G. KLATSKIN, and F. D. HUMM. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **213**, 31–36, Jan., 1947. 1 fig., 19 refs.

The 17-ketosteroid excretion in 27 of the patients with gynaecomastia described in Abstract 1888 was intermediate between the levels of excretion of normal women and normal men of the same age, and was significantly different from both normal groups. The average daily excretions were 8·4, 10·3, and 14·2 mg. Values for cortin excretion and follicle-stimulating gonadotrophin excretion were within normal limits. Although the oestrogen excretion values were also within normal limits they were near the lower limit and the ratio of 17-ketosteroid to oestrogen excreted was normal. A small group of civilian patients with gynaecomastia but receiving normal diets showed similar hormonal excretion values. The cause of the condition is still debatable. *Peter C. Williams*

1890. **Researches on Salivary Lipase.** (Untersuchungen über die Speichellipasen)
H. E. LURA. *Schweizerische Monatsschrift für Zahnheilkunde* [*Schweiz. Mschr. Zahnheilk.*] **56**, 920–926, Oct., 1946. 2 refs.

The author demonstrates the presence in the saliva of an enzyme capable of splitting up fats. This splitting up is considerable (45% in 3 to 4 hours for tributyrinase). The principal function of this enzyme appears to be that of cleansing the mouth, but it may also assist in digestion.
D. Robertson-Ritchie

1891. **Effect of the Fat Content of Diets on Blood Sugar**
M. SOMOGYI and R. J. COOK. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **65**, 336–339, June, 1947. 6 refs.

The post-absorptive venous blood sugar was determined in 10 healthy individuals at the Jewish Hospital of St. Louis. The patients were then given a high-fat (200 to 250 g. daily) low-carbohydrate (100 g.) diet. In

9 cases a distinct rise (6 to 13 mg. per 100 ml.) was observed in the post-absorptive venous blood sugar after 2 to 3 days. The change was readily reversed by a return to a normal diet, and was dependent on simultaneous intake of at least 100 g. carbohydrate daily. These changes were also seen, but in a more accentuated form, in diabetic patients, 400 of whom were studied.

S. S. B. Gilder

1892. **The Effects of Changes in Dietary Protein on the Composition and Structure of the Liver Cell**

H. W. KOSTERLITZ. *Journal of Physiology* [*J. Physiol.*] **106**, 194–210, June 2, 1947. 8 figs., 56 refs.

Rats were used as the experimental animals to investigate the chemical and cytological changes in liver cells after the administration of varying amounts of dietary protein. Whenever there is a deficiency in dietary protein the liver loses protein, phospholipin, and, to a less extent, nucleic acid. It is suggested that only cytoplasmic ribonucleic acid is affected and not the nuclear deoxyribonucleic acid. Alternatively, rats given a high-protein diet showed an increase of protein, phospholipin, and nucleic acid in their livers. It is shown that the changes in the liver protein are not caused by gains or losses of an inert storage protein, but by gains or losses of whole cytoplasm, both particulate and interparticulate matter being affected.

Rats were also fed on a protein-free diet for varying periods in order to study the rates at which protein, phospholipin, and nucleic acid were lost from the liver. It was found that of the initial liver cytoplasm, they lost 16·2% in 1 day, 23·8% in 2 days, 26·7% in 4 days, and 28·1, 33·1, and 39·6% in 1, 2 and 4 weeks respectively. Similar changes took place if the rats were fasted for 1 or 2 days. The loss is most rapid in the first few days and the author calls this easily lost fraction "labile" liver cytoplasm. The liver of the fasted rat has small but well-staining cells, described as "glycogen-poor hypocytoplasmic". In the rats fed on a protein-free diet the liver cells stained poorly ("glycogen-rich hypocytoplasmic"). In both types there is a profound loss of basophil granules and chromophil ground substance. The possible physiological significance of these changes in liver cytoplasm is briefly discussed.

A. I. Suchecki

VITAMINS

1893. **Influence of Vitamin B_1 on the Blood and Urinary Amylase of the Child.** (Influenza della vitamina B_1 sull'amilasi ematica ed urinaria nel bambino)

M. BOLLETTI and E. COSSANDI. *Pediatria del Medico Pratico* [*Pediat. Med. prat.*] **19–21**, 388–397, Sept., 1946. 26 refs.

After receiving an intramuscular injection of 12·5 mg. or 50 mg. of synthetic aneurine 3 hours after a meal 20 healthy boys, from 1 month to 8 years of age, showed a decrease during the subsequent 3 to 6 hours of, in some cases, 50% in the diastase content of the blood as estimated by a micro-Wohlgemuth method, with a return to the initial value in the course of 12 hours. Parallel with this a corresponding increase in the diastatic index of the urine was observed in 10 of the cases. Four boys, aged 4 months to 6 years, serving as controls and receiving no injection, showed a constant diastatic index in blood and urine throughout the day. It is suggested that the aneurine produces its effect by lowering the renal threshold for amylase.

T. R. Parsons

1894. **The Nervous System and Experimental Vitamin-A Deficiency.** (Sistema nervoso e avitaminose A experimental)

F. A. DE MOURA CAMPOS. *Revista Brasileira de Medicina* [*Rev. brasil. Med.*] **4**, 343–349, May, 1947. 1 fig., Bibliography.

Fifty investigations on experimental vitamin-A deficiency, published chiefly in American and British journals since 1914, are reviewed and the conflicting theories are briefly discussed. The author describes his own observations when 48 white rats, 30 to 40 days old, were given a vitamin-A-free diet of pure casein, starch, cocoa-butter, yeast, and salt solution for 3 months; 22 rats showed wasting and ataxia of the hind limbs, dorsal spinal curvature, and muscular spasm and tremors—changes which have more often been associated with vitamin-B deficiency than with a lack of vitamin A. Abnormalities of gait appeared from the fifty-sixth to the eighty-ninth day of the diet. He observed that ataxia developed even while the weight was still above the initial weight of the young rat; thiamine in doses of 33 to 66 μg. was ineffective, but vitamin A from butter and red-palm oil produced improvement in 2 out of 4 rats so treated; treatment with vitamin B and vitamin-B complex did not prevent the development of symptoms in 17 rats. Ocular manifestations varied in degree up to corneal ulceration. The details of the experiment are clearly analysed in two tables; the first gives the rat's age, initial weight, date of onset of ataxia, weight at onset, treatment, and symptoms; the second shows the relation between the animal's weight and the appearance of ataxia and of ocular symptoms. Ataxia followed loss of weight in 18 out of 22 animals, and coincided with it in 4; ocular symptoms preceded ataxia in 17 cases, followed it in 2, and were simultaneous in 3. From these results the author considers that neuromuscular changes are of no value in the early diagnosis of experimental avitaminosis A.

J. J. Keevil

1895. **Apparent Lack of Relationship Between Levels of B-vitamins in the Feces and Dietary Supplementation with Crystalline B-vitamins and Protein**

M. FREED, W. E. GRUNDY, C. R. HENDERSON, and G. H. BERRYMAN. *Gastroenterology* [*Gastroenterology*] **8**, 353–357, March, 1947. 1 fig., 7 refs.

Seven normal young volunteer male subjects ate for 38 weeks a diet which contained restricted quantities of B-vitamin and protein. Approximately 27% of the calorie intake was provided by cornmeal and other corn products. After 5 weeks 2 of the subjects were chosen as controls and thereafter were given crystalline B-complex

and protein supplements to equal the amounts usually found in a normal diet. No consistent relationship was found between this "complete" supplementation and the levels of fecal B-vitamins. The remaining 5 subjects were supplemented additively with individual B-vitamins and protein, beginning at 15 to 18 weeks. No consistent interrelationship was found to occur between any or all of these supplements and the levels of fecal B-vitamins, except possibly in the instance of pyridoxine. This latter possibility requires further investigation.—[Authors' summary.]

1896. **Epithelial Keratinization as Evidence of Fetal Vitamin A Deficiency**
J. G. WILSON and J. WARKANY. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **64**, 419–422, April, 1947. 4 figs., 3 refs.

The cardinal sign of vitamin-A deficiency is the appearance of stratified keratinized epithelium in an unusual site. The authors of this article describe such "keratinizing metaplasia" in sections of the genito-urinary tract taken from 14 rat foetuses and newborn rats whose mothers were kept on an A-deficient diet throughout pregnancy. Normally keratinization only takes place in the most distal parts of the urethra. Neither the controls nor the experimental animals showed any keratinization before the eighteenth day of gestation, but by the twentieth day a small area of truly keratinized epithelium was consistently found in the distal two-thirds of the urogenital sinus. More advanced changes were found on the twenty-first and twenty-second days (the latter were newborn rats); these are illustrated by photomicrographs of the urethra of a newborn rat whose mother had received adequate vitamin A and of the offspring of an inadequately fed mother. The latter shows a further degree of cornification and much desquamation at some points, metaplasia being most pronounced on the dorsal aspect of the urogenital sinus and genital ducts.

It is evident from these observations that vitamin A is necessary for the formation of normal genito-urinary epithelium in rats, but that a certain degree of differentiation is needed before metaplasia occurs on about the eighteenth day. *T. E. C. Early*

1897. **Excess Vitamin A Ingestion, Thyroid Size and Energy Metabolism**
D. P. SADHU and S. BRODY. *American Journal of Physiology* [*Amer. J. Physiol.*] **149**, 400–403, May 1, 1947. 1 fig., 5 refs.

Heavy vitamin-A medication, while allowing normal growth of rats, depressed their basal metabolism and reduced the weight of their thyroids. The excess vitamin A also depressed the thyroid size of thiouracil-treated rats. Heavy vitamin-A medication tends to neutralize the increased metabolic effect of thyroxine injection. While potassium iodide decreased somewhat the metabolic rate of control rats, it did not decrease the metabolism of the thyroxine-treated rats. Partly oxidized vitamin A reduced the thyroid size.

Several theories are suggested to account for the observed effects of excess vitamin-A ingestion in depressing the metabolic rate and thyroid size; the simplest is that the thyroxine iodine is taken up by the double bond of the vitamin A. This reaction annuls the metabolism-stimulating effects of thyroxine, and the resulting iodinated vitamin A, like thyroxine, depresses pituitary thyrotrophic hormone secretion, thereby reducing the size of the thyroid.—[From the authors' summary.]

1898. **Vitamin A Content in Human Liver**
L. DZIALOSZYŃSKI and W. TOMASZEWSKI. *Edinburgh Medical Journal* [*Edinb. med. J.*] **54**, 252–259, April–May, 1947. 2 figs., 15 refs.

Vitamin A and carotene were determined in the liver of 103 cases at necropsy and grouped according to the cause of death. The average findings (A=vitamin A in i.u.; C=mg. carotene per g. wet liver) were: accidental and sudden death, A 586, C 6·6; acute infections, A 603, C 5·7; neoplasms, A 545, C 5·4; liver disease, A 414, C 5·6; kidney disease, A 380, C 5·3; chronic infections, A 304, C 4·1; alimentary disease, A 208, C 4·0. The two highest vitamin-A values were 2,453 i.u. in a woman aged 49 with pneumonia and 2,270 i.u. in a man aged 77 with pyelocystitis. The three lowest values were: 1 i.u. in a girl, 16 years old, with organic heart disease; 10 i.u. in a man, 27 years old, with endocarditis; and 19 i.u. in a girl aged 17 with nephritis. The overall average vitamin A was 547 i.u. per g. wet liver, which is more than double the average value found by Moore in 900 livers in 1931–7; the values tended to be lower in persons under 20 years of age. *H. E. Magee*

1899. **A Study of Ascorbic Acid Metabolism of Adolescent Children**
C. A. STORVICK, M. L. FINCKE, J. P. QUINN, and B. L. DAVEY. *Journal of Nutrition* [*J. Nutrit.*] **33**, 529–539, May 10, 1947. 14 refs.

The mean plasma ascorbic acid value in 81 children living at a Children's Farm Home, 43 boys and 38 girls between the ages of 11 and 18, was 0·56 mg. per 100 ml. This value approximates to the standard (0·6 mg. per 100 ml.) considered adequate by the Committee on Vitamins of the American Academy of Pediatrics. It is noted that in 71% of the girls and 42% of the boys the value fell below this level.

Eight of these children (4 boys and 4 girls), aged 12 to 14 years, also served as subjects in a 3-week experimental study. All of the children were apparently healthy. The food they ate was weighed and recorded; samples of food presumed to contain ascorbic acid were analysed after each meal by the method of Loeffler and Ponting. Blood samples were taken daily before breakfast. During the first week the children ate the regular diet served in their cottage and were allowed second helpings. Ascorbic acid intake varied, as did the intake of all other constituents during this week, according to the inclination of each child. In this way the effect of the diet usually served and eaten on the ascorbic acid in the blood plasma could be observed. The second week

served as a saturation period. In addition to the regular diet, from which significant sources of ascorbic acid were removed and replaced by foods of low ascorbic acid content, the children received a supplement of 200 mg. of pure ascorbic acid just before breakfast. During the third week the ascorbic acid permitted from food was limited to 20 mg. per day, and the children received a supplement in order to bring the total daily intake to the amount recommended by the National Research Council, this supplement being 60 mg. for the girls and 55 to 70 mg. for the boys, according to age. The children were allowed to eat, *ad libitum*, bread, butter, meat, and other foods which contained no ascorbic acid.

While the boys' mean dietary intake for the first week was higher than that of the girls, 61 mg. as compared with 44 mg. of ascorbic acid per day, there was an even greater difference in their plasma levels, that of the boys being well within the range of adequacy, but that of the girls being markedly below. Peak values during the second week were about the same for both groups, but were reached sooner in the boys, whose levels dropped more abruptly when the intake was reduced. During the last 5 days of the third week all the children maintained mean plasma values varying around 0·9 mg. per 100 ml. These values were below those attained during the saturation period, but well above those considered adequate.

From a comparison of the results of this study with the researches of other investigators on adults and younger children, it is suggested that young adolescent boys and girls may require more ascorbic acid per kilo body weight to maintain tissue saturation than do younger children or adults. It is also suggested that it would probably be advisable during the strain of adolescent growth to maintain all values near saturation point; diets may well be planned to include the allowance recommended by the National Research Council.

Joseph Parness

1900. **The Renal Threshold for Ascorbic Acid. A Modified Method for its Estimation with Results for Twelve Adult Subjects**

A. M. KLOSTERMAN, J. E. HAINES, H. M. HAUCK, and A. B. KLINE. *Journal of Nutrition* [*J. Nutrit.*] **33**, 505–509, May 10, 1947. 4 refs.

The data on the renal threshold for ascorbic acid compiled by Lewis *et al.* (*J. Nutrit.*, 1943, **25**, 185) were obtained from subjects studied for 2-week periods by daily determination of fasting plasma ascorbic acid and corresponding urinary excretion values after 1 hour. The method of estimating the renal threshold was based on the "t" test of "Student" for determining the mathematical significance of the differences between means. In the course of daily determinations for 6-week periods in the same laboratory, the authors have evolved a modified method for treating such data. Blood samples were taken midway in the hour for which the urine specimen was collected. Some specimens were obtained under fasting conditions, and some after varying doses of ascorbic acid. The results give the values for the renal threshold for ascorbic acid in 12 adult subjects.

The data for plasma ascorbic acid values for each subject with the corresponding hourly urinary excretion values were assembled, and scatter diagrams were made. From inspection the apparent renal threshold for ascorbic acid was noted for each subject. The mean value, with its standard deviation, for urinary excretion of ascorbic acid at the apparent renal threshold was then calculated. This was compared with the mean value and standard deviation for urinary excretion at all plasma levels below the apparent renal threshold. Since, by definition, the renal threshold for ascorbic acid is the plasma concentration at which a marked rise in urinary excretion of ascorbic acid occurs, it follows that if the threshold value obtained by inspection is correct the excretion of ascorbic acid at this plasma value will be relatively large and variable; below the renal threshold the excretion is low and relatively constant. To test the validity of the apparent renal threshold similar calculations were made for plasma values 0·1 mg. per 100 ml. below and 0·1 mg. per 100 ml. above the apparent renal threshold.

For the 12 subjects the renal threshold values for plasma ascorbic acid as estimated by this method ranged from 1 to 1·3 mg. per 100 ml. Mean excretion values for ascorbic acid at the threshold were all above 2 mg. per hour, and most standard deviations were considerably more than half the mean. Inspection of the data for the entire series suggests that if a subject excretes 2 mg. or more of ascorbic acid in 1 hour his plasma ascorbic acid value has almost certainly exceeded his renal threshold during that hour, whereas if the excretion is 1 mg. or less it probably has not. On comparison of the findings with those of Lewis *et al.* the authors consider that the present modified method is simpler and has a wider range of utility.

In the present series 4 subjects were studied for 2 successive years. Evidence from the entire series suggests that the renal threshold for ascorbic acid is relatively stable in the normal adult from year to year and, within the limits of this experiment, at various levels of intake.

Joseph Parness

1901. **The Distribution of Ascorbic Acid in the Blood**

J. H. ROE, C. A. KUETHER, and R. G. ZIMLER. *Journal of Clinical Investigation* [*J. clin. Invest.*] **26**, 355–358, May, 1947. 3 figs., 14 refs.

UROGENITAL SYSTEM

1902. **Studies on the Biochemistry of Human Semen. I. The Natural Substrate of Prostatic Phosphatase.** [In English]

F. LUNDQUIST. *Acta Physiologica Scandinavica* [*Acta physiol. scand.*] **13**, 322–333, June 20, 1947. 22 refs.

In 1946 the author gave some evidence for the presence in ejaculated human semen of phosphoryl choline. The existence in semen of an alcohol-soluble substance, the calcium salt of phosphoryl choline chloride, is now demonstrated. The substance, of which the nitrogen/phosphorus ratio is 1, is stable against acid hydrolysis. The greater part of the phosphorus content of semen has been shown to be formed in the seminal vesicles, and it is

therefore inferred that the phosphoryl choline is secreted by these glands. On ejaculation the fluid from the vesicles is mixed with the prostatic secretion, the phosphatase of which soon causes splitting of the phosphoryl choline. Total splitting was assumed to have occurred in 1-day-old samples. About 80% of the total phosphorus could be accounted for as inorganic and phosphoryl choline phosphorus. Disintegration of phosphorus compounds in semen is extremely rapid. One sample, 1·5 minutes after ejaculation (at −10° C.), showed 21·6 mg. inorganic phosphorus per 100 ml. [Given by the author as m.% or thousands per cent. because he objects to the expression mg.%.] Eleven minutes after ejaculation (5 at −10° C. and 6 at 20° C.) it was 45·3 m%; and 20 minutes after ejaculation [presumably at 20° C.] it was 64·2 m%. Similar experiments on bovine semen showed much lower values for both phosphorus and choline. Evidence is given for the presence also in bovine semen of a compound liberating phosphorus and choline under the influence of enzymic activity. *D. T. Barry*

1903. **Elimination of Urea, Sodium, and Chlorine in the Supersaturated Urine and According to the Intensity of Diuresis.** (Las eliminaciones de urea, sodio y cloro por la orina con sobrecargas, y según la intensidad de la diuresis)

M. T. CANTERA, C. JÍMENEZ DÍAZ, and A. MERCHANTE. *Revista Clínica Española* [*Rev. clín. esp.*] **24**, 9–15, Jan. 15, 1947. 4 figs., 14 refs.

Ambard's view that urea and sodium chloride can simultaneously reach independent concentrations in urine in case of supersaturation, with dearth of water intake, is questioned. The osmotic pressure of total solids must be taken as the criterion of renal capacity, and the idea seems surprising that maximal concentration of sodium chloride should not hamper the elimination and concentration of other elements like urea. If the kidney cannot exceed a certain limit of osmotic concentration this must be so. Some recent workers have held that in the conditions mentioned chlorides and urea may vary inversely.

The present authors studied this problem in normal human subjects given varying amounts of water and a constant low-nitrogen diet and ingesting excess of urea or sodium chloride. They conclude that increased ingestion of sodium chloride with low water intake causes increase of urinary volume at the cost of water from the tissues, with increased elimination of sodium and chlorine, but with retention of a part in order to economize water. There is a well-marked diminution in the output of urea. The reverse holds when urea is given in excess. The sodium-chloride concentration at a given osmotic level can only increase at the cost of urea. There is a reciprocal inverse ratio. When enough water is ingested excess of the various salts is eliminated without bringing this function into play. The saline elimination with small amounts of water is the chief determining factor of urinary volume. In certain conditions the sodium and chlorine may be unequally excreted as in pathological states, and as seen from the action of suprarenal cortex. *D. T. Barry*

1904. **Some Endocrine Influences on Renal Function and Cardiac Output**

H. L. WHITE, P. HEINBECKER, and D. ROLF. *American Journal of Physiology* [*Amer. J. Physiol.*] **149**, 404–417, May 1, 1947. 1 fig., 21 refs.

From previous investigation of endocrine influence on glomerular filtration rate and on tubular excretion and output of urine, it was ascertained that " diodrast " (D) clearance and inulin plasma clearance drop permanently to 50 to 60% of normal after hypophysectomy. Maximum tubular excretion of diodrast (D Tm) drops within a few days to 50% and in a few weeks to 20 to 30% of normal. It is now found that thyroidectomy in dogs produces a drop in D clearance and D Tm, but much less than hypophysectomy. Thyroid administration raises D clearance and D Tm in these dogs. Anterior lobe extracts, which result in great increase in clearance of D and inulin in normal and hypophysectomized dogs, cause small and inconsistent rises in the thyroidectomized dog. Bilateral ovariectomy does not affect clearance of D or inulin or D Tm. Where there were large falls in D clearance and D Tm with a slight fall in inulin clearance due to very mild adrenal deficiency normal levels were restored by implantation of pellets of desoxycorticosterone acetate. Anterior lobe administration does not raise the clearance and D Tm in adrenal-deficient dogs as it does in hypophysectomized and normal animals. The falls in clearance and Tm values in hypophysectomy are not due to loss of thyrotrophic or gonadotrophic hormones, nor to the reduction of oxygen consumption *per se*.

The problem of how hypophysectomy influences renal function presents different possibilities: (*a*) loss of adrenotrophic hormone; (*b*) loss of a directly acting " renotrophic " hormone; (*c*) simple overall change in metabolism. The cardiac outflow is greatly and permanently diminished after hypophysectomy, the oxygen consumption and renal flow being reduced by a corresponding degree. *D. T. Barry*

NERVOUS SYSTEM

1905. **Differential Spinal Block. III. The Block of Cutaneous and Stretch Reflexes in the Presence of Unimpaired Position Sense**

S. J. SARNOFF and J. G. ARROWOOD. *Journal of Neurophysiology* [*J. Neurophysiol.*] **10**, 205–210, May, 1947. 1 fig., 6 refs.

Differential spinal block was induced in human subjects by injection of a solution of 0·2% procaine into the subarachnoid space. Vasomotor, sudomotor, and superficial pain fibres were blocked, while motor power, touch, position sense, and vibration sense were unimpaired. It has been generally thought that fibres subserving position sense and those subserving afferent impulses in the reflex arcs of knee- and ankle-jerks were of the same type (loosely called " stretch afferents "), but the results now obtained indicate that position sense and stretch reflex afferents are mediated by separate groups of fibres, for the block annulled the reflexes without affecting the others. If the differential blocking effect

in the subarachnoid space depends on the degree of myelination and axon diameter it can be concluded that the afferent paths of the reflex arcs just mentioned and of the abdominal reflex are subserved by relatively small unmyelinated fibres. Possible fallacies have to be taken into account in the interpretation of results. The knee-jerk is elicited by a single afferent volley from the hammer, while the postural afferent paths are subjected to repetitive stimuli which may cross a blocked region.

D. T. Barry

1906. **Effects of Ultraviolet Radiation on Visual Thresholds**
E. WOLF. *Science* [*Science*] **105**, 366, April 4, 1947. 1 fig., 3 refs.

After Wolf had shown that in both the chick embryo and the human eye ultraviolet radiation of wavelength longer than 285 mμ has a deleterious effect, Ludvigh and Kinsey demonstrated that the visual threshold light-difference and critical flicker frequency do not affect the fovea after exposure for 5 minutes to the radiation of a 1,000 watt mercury vapour arc from which almost all the ultraviolet radiation shorter than 320 mμ has been filtered out. The author points out that tests of foveal sensitivity do not exclude action on the peripheral rod units. A graph on the course of dark adaptation of the human eye, and for baby chicks after exposure to radiation from mercury vapour lamps, shows that in both cases the cone part of the duplex dark adaptation curves is unaffected by the pre-exposure to ultraviolet light, while the rod segments are clearly affected.

A. Sorsby

1907. **Pilometric Measurements and the Rheological Properties of Hair**
A. L. COPLEY. *Science* [*Science*] **105**, 340–342, March 28, 1947. 1 fig., 5 refs.

The author describes an instrument for measuring the firmness of attachment and the tensile properties of hairs by means of a tension-balance mechanism. The method is put forward as a possible aid in assessing results during treatment for baldness and other conditions affecting the hairs [a suggestion which dermatologists may regard as optimistic]. The chief use of the apparatus, and one of considerable interest to biochemistry, might well be the study of the effects of deficiency of known bodies, such as amino-acids, on the protein-molecular structure of hairs, or of hormones upon their viability.

Alex. Comfort

1908. **Effect of Parasympathetic Drugs on the Conditioned Response**
W. H. FUNDERBURK and T. J. CASE. *Journal of Neurophysiology* [*J. Neurophysiol.*] **10**, 179–187, May, 1947. 2 figs., 20 refs.

The action of acetylcholine on the central nervous system was investigated in cats in which conditioned responses had been set up. Efforts were made to influence the action of intrinsic acetylcholine by injection of eserine and prostigmin (anticholinesterases), magnesium sulphate, which blocks the action at myoneural junctions, and atropine, which inhibits the muscarine-like effects. Only eserine and prostigmin affected the responses; the former annulled them, apparently by inducing increase of acetylcholine in the brain (it caused no tenesmus); while prostigmin diminished the response, apparently because of the intestinal tenesmus produced, without influencing cholinesterase in the brain. Magnesium sulphate prevented the action of eserine. It was injected intraperitoneally (50 mg. per kilo). Given alone it did not affect the conditioned response. Pilocarpine (0·25 to 0·5 mg. per kilo) intravenously caused in the larger dose slight initial slowing and then facilitation of the reflex. Acetylcholine exerts a profound effect on the central nervous system, as indicated by the extinction of the conditioned response, but the mechanism of this action is somewhat obscure. There is a possibility that some side-action of eserine, rather than an increase of acetylcholine is the explanation of the extinction caused by it.

D. T. Barry

1909. **Acetylcholine and Synaptic Transmission in the Spinal Cord**
J. C. ECCLES. *Journal of Neurophysiology* [*J. Neurophysiol.*] **10**, 197–204, May, 1947. 2 figs., 18 refs.

The isolated spinal cord of the frog was used for testing the hypothesis that acetylcholine is a mediator of synaptic transmission in the central nervous system. Repetitive stimulation of the dorsal roots of the cord was carried out during the recording of synaptic potentials of the ventral roots. Prostigmin was used for abolition of cholinesterase activity, and then the cord was soaked in strong acetylcholine solution (6×10^{-3}M or even $1{\cdot}2\times10^{-2}$M). Prostigmin, like eserine, has no detectable effect on the synaptic potentials set up in the anaesthetized spinal cord by dorsal root volleys, even when they are rapidly repetitive. The depressant action of strong acetylcholine solutions on synaptic potential is about 0·002 that exerted on the end-plate potential. It is argued that as the cholinesterase will have been virtually inactivated these observations refute the hypothesis that acetylcholine mediates synaptic transmission.

[The suggestion of Funderburk and Case (Abstract 1908) that prostigmin does not perhaps affect the cholinesterase in the brain may be of some interest in this connexion.]

D. T. Barry

1910. **On the Lengthening and Shortening Reactions and their Occurrence in Man**
G. G. J. RADEMAKER. *Brain* [*Brain*] **70**, 109–126, June, 1947. 8 figs., 9 refs.

1911. **The Organization of the Motor Cortex of the Monkey based on Electromyographic Studies**
J. F. BOSMA and E. GELLHORN. *Brain* [*Brain*] **70**, 127–144, June, 1947. 13 figs., 7 refs.

1912. **The Hippocampus and the Sense of Smell. A Review**
A. BRODAL. *Brain* [*Brain*] **70**, 179–222, June, 1947. 5 figs., Bibliography.

Pharmacology and Therapeutics

1913. **Some Effects of Sodium Pentobarbital (Nembutal) and Allyl Methylbutyl Barbituric Acid (Seconal), at the Somatic Neuromyal Junction and on Skeletal Muscle.** [In English]
M. J. HUSTON, A. W. MARTIN, and J. M. DILLE. *Archives Internationales de Pharmacodynamie et de Thérapie* [*Arch. int. Pharmacodyn.*] **74**, 46–62, April 1, 1947. 35 refs.

"Nembutal" (pentobarbitone soluble, B.P.C.) and "seconal" (sodium 5-allyl-5 (1-methylbutyl) barbiturate) were added to defibrinated blood used to perfuse a dog's sciatic-gastrocnemius preparation. The effects upon the response of the muscle to stimulation, through the nerve and directly, were studied. A concentration of 50 mg. of drug per 100 ml. caused an increased response; 100 mg. per 100 ml. produced a preliminary increase followed by depression. Preparations were also made from dogs 3 to 5 days after division of the sciatic nerve. Stimulation of the partially degenerated nerve still produced some response, which was affected by the drugs in the same way as in normal preparations. Concentrations of drug which depressed the response to nerve stimulation enhanced the effect of direct stimulation of the muscle, and concentrations of 400 mg. of nembutal or 200 mg. of seconal per 100 ml. were required before depression of the direct stimulation occurred. It is estimated that five to eight times as much drug is required to depress the neuromyal junction as to depress central or autonomic synapses. *L. G. Goodwin*

1914. **Effect of Metrazol on the Electrical Excitability of the Respiratory Center When Depressed by Phenobarbital**
M. I. R. DE RAMIREZ DE ARELLANO. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **90**, 95–103, June, 1947. 4 figs., 14 refs.

Cats were anaesthetized by intravenous injection of 150 mg. of sodium phenobarbitone per kilo or were "decerebrated" by ligature of the carotid and basilar arteries. The threshold of electrical stimulation of the respiratory centre was then determined and a "depressant" dose of 90 to 160 mg. of phenobarbitone per kilo given. Intravenous administration of 50 to 300 mg. of "metrazol" per kilo caused in all cases a marked lowering of this threshold. In cats similarly "decerebrated", but not depressed by phenobarbitone, metrazol did not stimulate respiratory activity or lower the threshold.
V. J. Woolley

1915. **Selective Inhibition of Pseudocholinesterase by Di*iso*propyl Fluorophosphonate**
R. D. HAWKINS and B. MENDEL. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] **2**, 173–180, Sept., 1947. 18 refs.

1916. **The Influence of Morphine Hydrochloride on the Pancreatic and Biliary Secretion in Man.** [In English]
H. O. LAGERLÖF. *Acta Physiologica Scandinavica* [*Acta physiol. scand.*] **13**, 306–309, June 20, 1947. 3 refs.

Morphine decreases the delivery of bile and pancreatic juice to the duodenum. This is due, partly at least, to contraction of Oddi's sphincter. Morphine depresses the production of pancreatic enzymes.—[Author's summary.]

1917. **The Tracheal Chain. I. A Preparation for the Study of Antispasmodics with Particular Reference to Bronchodilator Drugs**
J. C. CASTILLO and E. J. DE BEER. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **90**, 104–109, June, 1947. 2 figs., 12 refs.

The trachea of a guinea-pig is cut transversely into twelve rings which are fastened together in a chain with silk. They are suspended in a bath of Van Dyke–Hastings solution and attached to a recording lever. Various drugs are added to the bath. Examples of the effects of adrenaline, aminophylline, papaverine, atropine, histamine, and "benadryl" are given.
V. J. Woolley

1918. **A Comparison of the Bronchodilator Activity of Benadryl with some of its Derivatives and Certain other Substances**
F. W. ELLIS. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **89**, 214–221; March, 1947. 2 figs., 8 refs.

In isolated and perfused guinea-pig lungs variations in outflow were expressed as percentages of the initial outflow, and used as quantitative indications of constriction or dilatation of the bronchi. A dose of 10 mg., of either "benadryl" or its monomethyl derivative, S-59, not only prevented the bronchoconstriction due to 0·1 mg., of histamine but consistently caused a dilatation of from 1·7 to 17%. This dilatation was less consistent after S-82, the *iso*propyl derivative of benadryl, and absent after S-92 (β-benzhydryloxyethyl trimethylammonium iodide) and S-158 (β-benzhydryloxyethyldimethylethyl ammonium *p*-toluenesulphonate), although all three substances completely antagonized the bronchoconstriction. Benadryl, S-59 and S-82 had similar actions on the spasm due to barium chloride or pilocarpine. S-154 (β-benzhydryloxyethyl trimethylammonium *p*-toluenesulphonate) and S-157 (4-β- benzhydryloxyethyl-4-methylmorpholinium *p*-toluenesulphonate) were quite active but failed to abolish consistently the effect of histamine. S-161 (β-benzhydryloxyethyl-β-hydroxyethylmethylamine) was the least active of the

benadryl series. Three other compounds unrelated to benadryl, S-150 (N-(*p*-tertiary-octylphenoxyethoxyethyl) morpholine), S-164 (N-β-hydroxypropylephedrine methiodide), and S-166 (N-β-hydroxypropylephedrine) had an insignificant antihistamine action.

In the vagotomized dog, either " spinal " or anaesthetized, the fall in blood pressure which followed intravenous injection of any " S " compound complicated the comparison of their activity in antagonizing bronchoconstriction due to histamine. A dose of 3 mg. per kilo of S-154 or S-59 given at the peak of bronchoconstriction appeared to relieve the spasm faster than did benadryl, though it is claimed that when the full effect of benadryl had developed it lasted longer. S-82 was the least effective under these conditions. When given prophylactically in a small number of animals (1 to 3 at each dose level), doses of 2, 3, and 5 mg. per kilo of benadryl protected the animals from the bronchoconstriction due to subsequent doses of 0·1 mg. per kilo of histamine for a longer time than similar doses of any of the other substances. The effects of S-154, S-59, and S-82 were much less persistent. *Derek R. Wood*

1919. **The Pharmacology of N-alkyl Homologues of Epinephrine**
A. M. LANDS, V. L. NASH, H. M. MCCARTHY, H. R. GRANGER, and B. L. DERTINGER. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **90**, 110–119, June, 1947. 3 figs., 9 refs.

The properties of the N-*sec.*-butyl homologue of adrenaline (" isuprel ") are described and compared with those of the already known N-*iso*propyl homologue. Both compounds cause a marked fall in blood pressure in the anaesthetized dog whether they are injected intravenously, intramuscularly, or into the lumen of the gut. They result in an increase in heart rate which is enough in the unanaesthetized dog to cause a transient rise in blood pressure. They give rise to bronchial dilatation equally with adrenaline, and relax the intestine and non-gravid uterus of rabbit and guinea-pig.
V. J. Woolley

1920. **Some Pharmacological Properties of Rutin**
R. H. WILSON, T. G. MORTAROTTI, and F. DEEDS. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **90**, 120–127, June, 1947. 3 figs., 23 refs.

Addition of 0·2 mg. of " rutin " (quercetin rhamnoglucoside) to a 50-ml. bath prolonged markedly the inhibitory action of adrenaline on a segment of guinea-pig colon, injections of 10 mg. of rutin increased the percentage of guinea-pigs surviving after histamine injection from 50 to 80–100 when histamine was given 10 to 30 minutes after the rutin. Rutin afforded no protection when given at the same time as the histamine. It is suggested that rutin protects adrenaline from oxidation, and that the consequent increase in blood adrenaline is the cause of its antihistamine action. Unsuccessful attempts were made to assay vitamin P by the capillary fragility method of Bacharach *et al.* (*Biochem. J.*, 1942, **36**, 407). *V. J. Woolley*

1921. **The Influence of Various Diuretics on the Urinary Sodium of Normal Pregnant Women**
W. E. BROWN and J. T. BRADBURY. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **32**, 312–313, March, 1947.

In pregnant women on a diet with constant sodium level administration of mercurial diuretics, ammonium chloride, aminophylline, or water (6 litres daily) increases daily sodium output. Administration of 25 to 50% glucose solution decreases it. Sodium concentration is greatest with the mercury compound and least with the water. *V. J. Woolley*

1922. **The Mercurial Diuretics: A Comparison of Acute Cardiac Toxicity in Animals and the Effect of Ascorbic Acid on Detoxification in their Intravenous Administration**
D. W. CHAPMAN and C. F. SHAFFER. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **32**, 313–314, March, 1947.

Lethal doses of " mercupurin ", " salyrgan " with theophylline, or " mercuhydrin " were given to dogs, with or without the addition of ascorbic acid. All the dogs which received mercupurin or salyrgan died of ventricular fibrillation and the lethal dose was not modified by addition of ascorbic acid. The dogs which received mercuhydrin died of ventricular asystole, and the lethal dose was increased over 50% if ascorbic acid was given beforehand or simultaneously. It is suggested that in man 2 ml. of mercuhydrin with 500 mg. of ascorbic acid is a suitable dose. *V. J. Woolley*

1923. **Mercurial Diuretics. A Comparison of Acute Cardiac Toxicity in Animals and the Effect of Ascorbic Acid on Detoxification in Their Intravenous Administration**
D. W. CHAPMAN and C. F. SHAFFER. *Archives of Internal Medicine* [*Arch. intern. Med.*] **79**, 449–456, April, 1947. 3 figs., 14 refs.

The toxicity of mercurophylline, mersalyl and theophylline, and " mercuhydrin " was investigated in dogs. The animals were maintained in anaesthesia with a 2·5% solution of pentobarbitone sodium and were connected with an artificial respirator. In the controls the drugs were injected into the femoral vein in doses of 1 ml. at intervals of 2 and 5 minutes. Ascorbic acid was given in doses of 150 mg. 10 minutes before injection of 1 ml. of mercuhydrin at 2-minute intervals, and 250 mg. was mixed with 1 ml. of each of the drugs and given simultaneously at 2- and 5-minute intervals. Electrocardiographic records were obtained before and during the injection. Bradycardia of less than thirty beats per minute, or ventricular asystole, or ventricular fibrillation was taken to indicate a lethal dose. With mercurophylline, mersalyl and theophylline, and mercuhydrin in that order, the minimum lethal dose (M.L.D.) at 2-minute intervals (6 dogs) was 0·29, 0·52, and 1·14 ml. respectively, and at 5-minute intervals (5 dogs) 0·14, 0·52, and 1·52 ml. When ascorbic acid was given simultaneously with mercuhydrin, the M.L.D. at 2-minute intervals (7 dogs) was 1·74 ml., and at 5-minute intervals (5 dogs) 2·47 ml.

When ascorbic acid was given 10 minutes before injection of mercuhydrin at 2-minute intervals the M.L.D. (5 dogs) was 1·69 ml. The toxicity of the other two drugs was not influenced by ascorbic acid. Thus, mercuhydrin was the least toxic of the three drugs, and the administration of ascorbic acid before, or simultaneously with, mercuhydrin reduced its toxicity. With or without ascorbic acid, death following mercuhydrin was due to ventricular asystole, and death following mercurophylline, or mersalyl and theophylline, was due to ventricular fibrillation. In 20 patients with cardiac failure 2 ml. of mercuhydrin mixed with 500 mg. of ascorbic acid and given intravenously resulted in an equal or an increased diuresis up to 50%. *J. L. Markson*

PENICILLIN

1924. **Studies in the Oral Administration of Penicillin. I. Assays of Various Preparations and the Determination of the Effective Therapeutic Dose**
W. S. HOFFMAN and I. F. VOLINI. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **213**, 513–519, May, 1947. 10 refs.

This paper reports the levels of penicillin in plasma achieved with varying doses of penicillin given orally. The estimations of the plasma concentration of the drug were made by the *Bacillus subtilis* serial dilution method, and the subjects were convalescent hospital patients. No antacid substances or buffers were given along with the penicillin. A satisfactory plasma penicillin level was taken to be a minimum of 0·03 unit per ml. at any time and 0·06 unit per ml. or higher most of the time. By these criteria it was found that doses of 25,000 units of penicillin given orally were ineffective. Doses of 50,000 units administered orally every 2 hours, though frequently effective, were unreliable in maintaining satisfactory levels in comparison with ordinary parenteral therapy. With an initial oral dose of 200,000 units followed by 100,000 units every 3 hours the plasma levels of the drug were satisfactory and comparable with those obtained after intramuscular injections of 20,000 units every 3 hours. *D. M. Dunlop*

1925. **Studies in the Oral Administration of Penicillin. II. Results of Treatment of Pneumococcic Lobar Pneumonia and other Acute Infections with Several Oral Penicillin Preparations**
W. S. HOFFMAN and I. F. VOLINI. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **213**, 520–534, May, 1947. 4 figs., 5 refs.

Forty-nine patients suffering from pneumococcal lobar pneumonia and 81 from miscellaneous infections due to penicillin-sensitive organisms were treated with penicillin administered orally. An initial dose of 200,000 units was given, then 100,000 units every 3 hours. As had been anticipated from previous assays the plasma penicillin levels on this dosage seldom fell below 0·06 units per ml. and were usually higher. This treatment successfully banished the systemic manifestations of pneumonia within 48 hours in 77% of the cases of pneumonia. In the remaining 23% there was failure because: (*a*) the illness was not due to a penicillin-sensitive organism but to a virus; (*b*) the pneumococcus involved was of an unusually resistant strain; (*c*) complications such as severe bronchitis developed, especially in elderly patients. In a few cases only was failure due to inadequate absorption of the drug. The patients with miscellaneous infections responded well to oral penicillin. In the authors' opinion the results were comparable with those obtained by the parenteral administration of penicillin in ordinary doses. The severity of the infection bore no relation to the required dosage of penicillin. The sensitivity of the organism was the determining factor in this respect. Urticaria occurred in 3·8% of the cases. When pure preparations of the drug were used such toxic manifestations were very rare. *D. M. Dunlop*

1926. **Penicillin Production by a Thermophilic Fungus**
L. J. RODE, J. W. FOSTER, and V. T. SCHUHARDT. *Journal of Bacteriology* [*J. Bact.*] **53**, 565–566, May, 1947. 1 ref.

A thermophilic fungus, tentatively identified as *Malbranchea pulchella*, has been found to produce penicillin at 52° C. In surface cultures maximum activity was reached on the fourth or fifth day at this temperature; maximum potency was about 5 i.u. per ml. Reasons are given for identifying this antibiotic as penicillin. *G. Payling Wright*

1927. **The Relation Between Induced Resistance to Penicillin and Oxygen Utilization**
W. D. BELLAMY and J. W. KLIMEK. *Journal of Bacteriology* [*J. Bact.*] **53**, 374–375, March, 1947.

After 64 transfers a strain of *Staphylococcus aureus* had its resistance to penicillin increased 60,000 times. This strain also lost its ability to grow anaerobically, while its rate of aerobic growth was from one-half to two-thirds that of the penicillin-sensitive parent strain. Under similar conditions three other organisms, *Streptococcus faecalis*, *Str. agalactiae*, and *Clostridium perfringens* developed very slight resistance to penicillin: the resistance of *Str. faecalis* was increased only 11 times in 47 transfers, that of *Str. agalactiae* 6 times in 24 transfers and that of *Cl. perfringens* 10 times in 25 transfers. It is suggested that penicillin interferes with some anaerobic metabolism. Organisms which are unable to develop or utilize an alternative energy mechanism do not become resistant to penicillin. *G. M. Findlay*

1928. **Discrepancy in Analysis of Penicillin in Blood by the Oxford Cup Method as Revealed by the Paper Disc Technique**
M. B. SHERWOOD and E. J. DE BEER. *Science* [*Science*] **105**, 414, April, 1947. 2 refs.

With *Bacillus subtilis* as the test organism it was found that solutions of penicillin in blood gave much lower results by the Oxford cup method than by the paper disk assay. When a standard solution of penicillin was

added to defibrinated rabbit blood, oxalated blood, or serum, results by the former method were only 33·5 to 66·6% as compared with 89·5 to 97·6% by the latter method. Similar discrepancies between the cup and disk techniques were observed when dog blood was used instead of rabbit blood. *R. Wien*

1929. **On the Mode of Action of Penicillin**
L. O. KRAMPITZ, M. N. GREEN, and C. H. WERKMAN. *Journal of Bacteriology* [*J. Bact.*] **53**, 378–379, March, 1947.

The authors, working at the Industrial Science Research Institute, Iowa State College, Ames, Iowa, describe an inhibitory effect of penicillin on the oxidation by *Staphylococcus aureus* of nucleic acids or nucleotides. The reaction inhibited by penicillin has an R.Q. of 1·0; the measurable end-products being carbon dioxide and acetic acid in a ratio of 3 : 7. Since 3 moles of oxygen are necessary the oxidation of a pentose is postulated according to the equation

$$C_5H_{10}O_5+3O_2\longrightarrow CH_3COOH+3CO_2+3H_2O.$$

Sodium ribonucleinate on oxidation by *Staph. aureus* shows the same ratio of end-products and this reaction also is inhibited both by penicillin and by streptomycin. Penicillin has no effect on glucose oxidation or on the utilization of the constituents of a synthetic medium on which good growth can be obtained. *G. M. Findlay*

1930. **The Penicillin Produced by *Aspergillus parasiticus***
H. R. V. ARNSTEIN and A. H. COOK. *British Journal of Experimental Pathology* [*Brit. J. exp. Path.*] **28**, 94–98, April, 1947. 12 refs.

" Parasiticin," an antibiotic produced under selected conditions by *Aspergillus parasiticus*, has been shown on biological and chemical evidence to be largely, if not wholly, penicillin-II (G) (benzylpenicillin); the distinctive name should be abandoned.—[Authors' summary.]

1931. **The *in vivo* Activity of Penicillin Esters**
J. UNGAR. *British Journal of Experimental Pathology* [*Brit. J. exp. Path.*] **28**, 88–93, April, 1947. 6 refs.

Esters of penicillin are known to be more stable than its salts, and it has been suggested that their slower absorption and excretion might offer further therapeutic advantages. The author has tested the *in vivo* activity of the pure methyl and benzyl esters of penicillin.

The methyl ester is crystalline and the benzyl ester is a yellow oil. Both are insoluble in water but soluble in arachis oil and fat solvents; they are stable for many months. Neither is biologically active *in vitro*. Well-controlled experiments showed that sodium penicillin and the penicillin methyl ester, both injected in oil, were equally effective in protecting mice against haemolytic streptococci. On the other hand, when the methyl or benzyl ester was injected into rabbits only negligible amounts of penicillin appeared in the blood and urine. The difference was due to the fact that mouse, but not rabbit, plasma contains an esterase which hydrolyses the ester and liberates free penicillin. Rats and guinea-pigs also possess the esterase, but man does not. Human volunteers had no penicillin in the blood after either intramuscular injections or oral administration of penicillin methyl ester. It is concluded that penicillin esters are unlikely to be of therapeutic value in man.

The plasma esterase afforded a convenient technique for the quantitative estimation of penicillin esters in fluids. Hydrolysis by the esterase liberated free penicillin, which could be estimated by the usual bacteriological techniques. *Martin Hynes*

1932. **Studies on Penicillinase. III. The Effect of Anti-penicillinase on Penicillin-resistant Organisms**
R. D. HOUSEWRIGHT and R. J. HENRY. *Journal of Bacteriology* [*J. Bact.*] **53**, 241–247, Feb., 1947. 1 fig., 16 refs.

Antipenicillinase serum was prepared by the injection of penicillinase into rabbits. Assays were made by incubating the penicillinase with dilutions of immune serum; precipitation was observed up to a dilution of serum of 1 in 56. The activity of penicillinase was completely destroyed by an hour's contact with dilutions of the antiserum of 1 in 112 and the activity was reduced with dilutions of 1 in 896. By a highly specific manometric method it was found that a dilution of 1 in 128 of serum caused a 90% loss of activity of the enzyme. The immune serum was only effective *in vitro* against organisms which produce extracellular penicillinase; its effectiveness with these was not sufficient to render them sufficiently susceptible to be classed as penicillin-sensitive. With the two strains of extracellular penicillinase producers tested, one of *Staphylococcus aureus* and one of *Bacillus cereus*, the effect of the serum was merely to halve the concentration of penicillin required for inhibition. The clinical usefulness of the immune serum appears doubtful, except possibly in mixed infections where the penicillinase produced by a secondary invader might be sufficient to render the primary infecting organism insusceptible. *G. A. H. Buttle*

1933. **The Relation of Natural Variation in *Penicillium notatum* to the Yield of Penicillin in Surface Culture**
A. J. WHIFFEN and G. M. SAVAGE. *Journal of Bacteriology* [*J. Bact.*] **53**, 231–240, Feb., 1947. 7 figs., 10 refs.

A high-yielding strain of *Penicillium notatum* will rapidly lose its high-yielding capacity if it is continuously subcultured. This loss of yield is due to the production of rapidly growing, low-yielding mutants which quickly outgrow the parent strain. This production of mutants is associated with spore formation, and spore formation can be kept down either by blending early cultures before sporulation has occurred or by serial seeding from submerged culture when surface growth is prevented by daily shake down. When spore formation is reduced to a minimum by either of these methods serial subculture does not reduce the yield of the strain. Continuous selection of high-yielding clones does not improve the yield of either high- or low-yielding strains.
G. A. H. Buttle

1934. **The Action of Penicillin and Tyrothricin on the Adenosine Pyrophosphatase of Muscle Extracts.** (Action de pénicilline et de la tyrothricine sur l'activité adényl pyrophosphatasique des extraits de muscles)
F. Gros and M. Macheboeuf. *Comptes Rendus de l'Académie des Sciences* [*C.R. Acad. Sci., Paris*] **224**, 1736–1738, June 16, 1947. 8 refs.

Penicillin has already been shown to inhibit very strongly the hydrolysis of adenosine triphosphoric acid by suspensions of non-proliferating *Clostridium sporogenes*. Neither penicillin nor tyrothricin shows any inhibitory action on the dephosphorylation of adenosine triphosphoric acid by muscle extracts. *G. M. Findlay*

1935. **The Interaction of Antagonistic Complexes of Cultures of *Penicillin notatum* and *Actinomyces griseus*.** (Réaction entre les complexes antagonistes issus des cultures de *Penicillium notatum* et d'*Actinomyces griseus*)
G. Ramon and R. Richou. *Comptes Rendus de l'Académie des Sciences* [*C.R. Acad. Sci., Paris*] **224**, 1605–1606, June 9, 1947. 1 ref.

A crude filtrate of *Penicillium notatum* does not inhibit the antibiotic action of a filtrate of *Actinomyces griseus*, but the antibiotic action of a filtrate of *P. notatum* is largely inhibited by the actinomyces filtrate. This inhibition is due to the presence of a penicillinase-like enzyme which can be destroyed by the action of chloroform. *G. M. Findlay*

1936. **Urticarial Reactions to Intramuscular Penicillin. A Report of Four Cases**
L. Steingold. *Lancet* [*Lancet*] **1**, 868–869, June 21, 1947. 10 refs.

In 4 cases intramuscular penicillin caused urticaria. The results of intradermal tests with pure and commercial penicillin suggest that this was an allergic response to an impurity in the commercial preparations. Controls showed no skin sensitivity to any of the penicillin preparations. In 2 of the cases dermatographia was observed.—[Author's summary.]

1937. **Epileptogenic Effects of Penicillin. An Experimental Study**
C. Pilcher, W. F. Meacham, and E. R. Smith. *Archives of Internal Medicine* [*Arch. intern. Med.*] **79**, 465–472, April, 1947. 5 figs., 6 refs.

Dogs were used in this experimental study. A small metal cannula was screwed into an opening in the skull in the left parietal area so that it just reached the dura. Subsequently, sodium penicillin in a solution of 1,000 units per 0·1 ml. was injected 2 to 3 mm. beneath the cerebral cortex. Epileptiform convulsions occurred after injection of 450 units or more, terminating fatally when 1,000 units was injected. By the intracisternal route the critical epileptogenic dose was 7,500 units, fatal convulsions following the injection of 15,000 units and 25,000 units. Intracisternal penicillin induced a pleocytosis in the cerebrospinal fluid. In another series of animals a moderate degree of hydrocephalus was first produced by intracisternal injection of lampblack. Subsequent injection of penicillin into the lateral ventricle in doses of 3,000 to 5,000 units was followed by convulsions; results were similar when crystalline penicillin was used. In control experiments with injection of isotonic saline and an autoclaved solution of penicillin the results were negative. It is pointed out that much lower dosage is normally employed intrathecally in the human subject, and that the dog is particularly susceptible to epileptogenic agents of other types. *J. L. Markson*

1938. **Demonstration of Hormesis (Increase in Fatality Rate) by Penicillin**
W. A. Randall, C. W. Price, and H. Welch. *American Journal of Public Health and the Nation's Health* [*Amer. J. publ. Hlth*] **37**, 421–425, April, 1947. 10 refs.

Garrod (*Brit. med. J.*, 1945, **1**, 107) pointed out that an increase in concentration accelerates the action of all common disinfectants but not of penicillin. The authors found that streptomycin increased rather than decreased the fatality rate in mice infected with *Salmonella typhi*. This effect has been described as " hormesis "—namely, a stimulation in growth of otherwise sensitive organisms by certain concentrations of antibiotic substances. Investigating the action of penicillins G and K on groups of white mice infected with *S. typhi* the authors find that, at certain levels of concentration, these drugs cause a similar increase in the death rate; this increase is not due to impurities. Mice which recovered showed an increased immunity to the organism. *John T. Ingram*

1939. **Sensitization to Penicillin**
J. G. Hopkins and H. Lawrence. *Journal of Allergy* [*J. Allergy*] **18**, 251–262, July, 1947. 2 figs., 7 refs.

STREPTOMYCIN

1940. **Mode of Action of Streptomycin on Type B *Hemophilus influenzae*. I. Origin of Resistant Organisms**
H. E. Alexander and G. Leidy. *Journal of Experimental Medicine* [*J. exp. Med.*] **85**, 329–338, April 1, 1947. 21 refs.

Organisms resistant to streptomycin were shown to be the cause of failure in the treatment of type B *Haemophilus influenzae* infection. Of 14 patients receiving streptomycin only, 10 recovered promptly; 3 of the other 4 infections proved to be due to resistant organisms. The question arises whether this failure is due to the presence in the bacterial population of streptomycin-resistant organisms or to metabolic adaptation. The demonstration of organisms resistant to 1,000 units of streptomycin per ml. in 10 strains of type B *H. influenzae*, including those isolated from patients who responded to streptomycin treatment, constitutes convincing evidence that in all bacterial populations there is a small number of resistant organisms. It seems that in all populations of *H. influenzae* there exist initially organisms with many different degrees of resistance. Thus the numbers able to grow in 1,000 units of the drug per

ml. are so small as to be detectable only with large inocula, whereas those which can thrive in 3 units per ml. are numerous enough to be detectable in much smaller populations. In an example cited, approximately 50 billion organisms were seeded into melted Levinthal agar containing only 10 units of streptomycin per ml. Fourteen colonies appeared after incubation for 72 hours; 9 of these, when tested after one subculture on streptomycin-free medium, proved resistant to 1,000 units per ml.; growth of 4 others was completely prevented by 100 units per ml. and of one by 50 units per ml. When the same inoculum was seeded into Levinthal agar containing 1,000 units per ml., 7 colonies grew within 72 hours. Samples of initial bacterial populations showed resistant members in all ten strains examined, the incidence varying from 1 in 1·1 billion to 1 in 13·8 billion organisms. The proportion of resistant organisms is not significantly higher before treatment in patients who prove refractory, than in those who respond promptly.

The authors conclude that resistance is the result of a selective process, and that the survival of highly resistant organisms, either in the patient or *in vitro*, is influenced more by the size of the bacterial population than by any other known factor. Further evidence that resistance is inherited is given by the fact that one resistant strain has been transmitted *in vitro* without change in degree through over 100 subcultures in streptomycin-free medium. Also, resistant organisms were found to persist in the nasopharynx of one patient over a period of one year. This latter observation is significant and raises an important public health problem.

Margaret Buchanan

1941. **Mode of Action of Streptomycin on Type B *Hemophilus influenzae*. II. Nature of Resistant Variants**

H. E. ALEXANDER and G. LEIDY. *Journal of Experimental Medicine* [*J. exp. Med.*] **85**, 607–621, June, 1947. 8 refs.

Streptomycin-resistant strains of *Haemophilus influenzae* type B arise both *in vivo* and *in vitro*, and the present paper presents evidence that these are derived from mutant organisms. Very large populations of bacteria (of the order of 2×10^{11}) must be used, however, to demonstrate the development of resistant strains, for the mutation rate is low. This finding conforms with clinical experience that resistant strains of this bacterial species only arise in severe infections. The criteria accepted in this paper for distinguishing mutants were: (1) evidence for the random occurrence of variants showing great differences in prevalence in different independent cultures of the same strain; (2) a low constant rate of occurrence which is consistent with mutation frequency; (3) transmissibility of the variant trait through many generations.

Ten strains of *H. influenzae* were used in this study. Bacterial counts were made of the resistant organisms in both genetically heterogeneous and homogeneous cultures—that is, progeny of single cell colonies. The irregular appearance of new resistant variants in repeated subcultures is consistent with the mutation theory. It was possible from the data collected, with the aid of a simple formula, to determine the mutant rate for each of the ten strains. The rate varied from $2{\cdot}6\times10^{-11}$ to 7×10^{-11} per bacterium per bacterial generation. These rates are closely similar in both genetically heterogeneous and homogeneous strains. Subcultures of 440 streptomycin-resistant strains showed that this character was a transmissible variant. Some strains were carried through 39 subcultures in the absence of streptomycin, yet they retained their property of resistance to the end. Two different types of variant were, however, noted; the first grew equally well in the presence of a high concentration of streptomycin and when it was absent, while the second grew better in the presence of the antibiotic. *G. Payling Wright*

1942. **Studies in Streptomycin. I. Factors Influencing the Activity of Streptomycin**

S. BERKMAN, R. J. HENRY, and R. D. HOUSEWRIGHT. *Journal of Bacteriology* [*J. Bact.*] **53**, 567–574, May, 1947. 1 fig., 14 refs.

Experiments were carried out to ascertain whether certain controllable variables affect the activity of streptomycin, so that standard methods for its assay may be improved. The growth-inhibitory power of streptomycin for a wide variety of bacteria was much reduced in the presence of sodium chloride and certain other salts at concentrations varying from 0·5 to 2%. The size of the inoculum affected greatly the subsequent growth of bacteria in the presence of streptomycin—the larger the number introduced the sooner multiplication began at any given concentration of the drug. It is considered that this phenomenon is due to the occurrence of occasional streptomycin-resistant bacteria and the likelihood of including any of these would increase with the number inoculated. The presence of horse serum in the medium did not affect the inhibitory power of streptomycin; the latter was found, however, to decrease with increasing acidity of the medium. *G. Payling Wright*

1943. **Studies on Some Biological Aspects of Dihydrostreptomycin**

R. DONOVICK and G. RAKE. *Journal of Bacteriology* [*J. Bact.*] **53**, 205–211, Feb., 1947. 1 fig., 12 refs.

Dihydrostreptomycin is formed from streptomycin by reduction with hydrogen. Its activity *in vitro* against most micro-organisms is similar to that of streptomycin, but there are slight differences in some cases. The toxicities to mice and the rates of excretion of both compounds are similar. It is uncertain whether dihydrostreptomycin acts without previous chemical change or whether it is first converted into streptomycin before its antibiotic effect is produced. *G. A. H. Buttle*

1944. **Streptomycin II, an Antibiotic Substance Produced by a New Species of Streptomyces**

D. B. JOHNSTONE and S. A. WAKSMAN. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **65**, 294–295, June, 1947. 5 refs.

1945. **Streptomycin in the Treatment of Pyocyaneus Infections of the Urinary Tract**
L. H. SCHWARZ and J. A. LAZARUS. *Journal of Bacteriology* [*J. Bact.*] **53**, 128, Jan., 1947.

Eight patients with pyocyaneus infections of the urinary tract have been treated with streptomycin. The susceptibility of the organisms varied from 12·5 to 250 units, the greatest resistance to streptomycin being shown by the mucoid variants present in 2 cases. Of the 6 cases caused by non-encapsulated organisms 2 only were cured after a dosage of 8,000,000 units, while for full effectiveness 13,000,000 to 20,000,000 units are required. Streptomycin caused a change of the mucoid strain to the rough phase with a reduction in virulence, but as soon as treatment ended the process was reversed and virulence was regained.

G. M. Findlay

1946. **Toxicity of Streptomycin**
W. MCDERMOTT. *American Journal of Medicine* [*Amer. J. Med.*] **2**, 491–500, May, 1947. 11 refs.

The toxicity of streptomycin can be considered under six headings. First, the so-called " histamine " reaction can now be attributed to impurities in the early preparations as can the second reaction, local inflammation at the site of injection. Thirdly, an intrathecal dose of more than 0·1 g. will, as a rule, cause a pleocytosis in the cerebrospinal fluid, with headache, somnolence, vomiting, and nystagmus. Anaphylaxis gives rise to a fourth group of toxic phenomena, which includes a characteristic fever, a morbilliform rash, a blotchy erythema, conjunctivitis, or simple eosinophilia. These manifestations are seen in a small proportion of cases even with highly purified streptomycin. The fifth toxic process is renal damage, which again may occur with highly purified streptomycin. The lesion may appear as a simple cylindruria worse in acid urine and possibly prevented by alkalis, or there may be definite impairment of renal function of nitrogen-retention type. It would seem that the latter is more liable to occur in kidneys already inefficient. The sixth and best known toxic reaction is a " neurological " one, and is probably not located in the eighth nerve but in the brain. There are two forms which may be seen in a high proportion of patients given 1 or 2 g. daily for a month. The first form is " vestibular dysfunction ", comprising dizziness, uncomfortable feelings of heaviness in the head, and nausea. The second form is bilateral deafness, of which a significant number of cases have been seen in fairly large series of cases studied. Both forms of " neurological " toxic disturbance may be related to excessive dosage, the presence of chronic renal disease or of meningitis, and the use of the intrathecal route. Finally, a few unclassified and miscellaneous toxic manifestations have been recorded, but there is no evidence, as yet, that streptomycin will damage the liver.

Whether the clinician should persist in giving streptomycin in the face of toxic manifestations is a matter for individual judgment with special regard to the prognosis if the treatment be discontinued. It would seem that the majority of the toxic manifestations likely to be encountered clinically in future are due to streptomycin itself and not to impurities, as in the early trials. Moreover, it would appear that these toxic manifestations, except deafness, are very largely reversible, in that they disappear, or tend at least to subside, when the treatment is stopped. Streptomycin can be said to be of low toxicity on the whole, but individual susceptibility varies greatly. A rough rule, so far as the admittedly incomplete information can at present serve as a guide, is that 3 g. is the maximum safe daily dose. *G. F. Walker*

SULPHONAMIDES

1947. **Sulfonamide Drugs. A Comparison of Blood Levels Obtained with Their Administration by Different Routes in Children**
G. H. CLARKE. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **73**, 565–572, May, 1947. 3 figs., 18 refs.

The author compares the results of various methods of administration of sulphonamide drugs to 56 patients aged from 2 months to 12 years. The initial dose was gr. ½ (32 mg.) per pound (0·45 kg.) of body weight, followed by a maintenance dose of gr. 1 (65 mg.) per pound body weight, divided into 4 or 6 aliquot parts in 24 hours in both oral and subcutaneous administration. For subcutaneous administration a 5% solution of the sodium salt in distilled water was used. Sulphadiazine was the drug employed in all these cases. In 4 children the implantation of sulphanilamide crystals intraperitoneally at operation was studied. The author concludes that subcutaneous administration of sodium sulphadiazine causes hardly any local reaction; that it is simpler than, and just as effective as, the intravenous route; that the hourly levels showed less fluctuation after subcutaneous than after intravenous injection; that somewhat higher levels were obtained in the blood by subcutaneous injection than by oral administration: and that the levels could be maintained for at least 2 weeks without alteration of dosage. Age did not appear to be a factor in determining the blood level obtained provided the dosage was regulated by body weight. The results of sulphanilamide implantation in the peritoneal cavity suggest that gr. 1 to 2 (65 to 130 mg.) per pound body weight gives safe and satisfactory blood levels. *R. E. Bonham-Carter*

1948. **The Absorption and Elimination of Sulfadiazine Administered as Tablets, as a Ground (Micronized) Powder and as Microcrystals**
E. M. BOYD and R. W. DINGWALL. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **213**, 549–556, May, 1947. 1 fig., 3 refs.

This paper suggests that the smaller the particle of sulphadiazine administered orally the faster will the drug be absorbed and eliminated. Sulphadiazine was given to 90 healthy volunteers in three forms, each form being given to 30 of the subjects. The first preparation consisted of sulphadiazine tablets as sold on the open market; the second of sulphadiazine reduced by grinding to small spheres, somewhat larger than microcrystals; the third

was microcrystalline sulphadiazine. The two last preparations were suspended in an aqueous vehicle containing volatile oils with flavouring and colouring agents. Four grammes of the drug was given with a pint of water to each subject and samples of blood and urine were examined at intervals up to 6 hours after the administration. Sulphadiazine was found to be most rapidly absorbed when given as microcrystals, and least rapidly in the form of tablets. At the end of 6 hours the concentration of sulphadiazine in the blood was the same whatever the form of administration. The combined sulphadiazine in the blood did not reach appreciable values for about 6 hours after administration, and the concentration was less marked after tablets had been taken. Further, sulphadiazine given in the form of tablets seemed to pass less readily from the plasma into the red blood cells than when given in the other two forms. The concentrations of total free and combined sulphadiazine in the urine roughly paralleled the blood values. *D. M. Dunlop*

1949. **The Effect of Sodium and Potassium Lactates upon the Absorption and Elimination of Microcrystalline Sulfadiazine.**
E. M. Boyd and R. W. Dingwall. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **213**, 557–561, May, 1947. 4 refs.

The authors point out several disadvantages from the use of sodium bicarbonate, commonly employed to render the urine alkaline during sulphonamide therapy, especially if it is added to an aqueous preparation of a sulphonamide, such as the suspension of microcrystalline sulphadiazine. They have therefore studied the effect on absorption and excretion of suspensions of microcrystalline sulphadiazine to which had been added respectively 8·5 g. of sodium and potassium lactate per 100 ml. of the suspension. The lactates were found to accelerate the absorption of the sulphadiazine microcrystals and gave higher initial concentrations in the blood and plasma. They also accelerated the excretion of the drug in the urine and increased the *p*H of the latter. Of the two preparations the sodium lactate was more effective and palatable than the potassium salt.
D. M. Dunlop

1950. **The Absorption of Some Sulphaguanidine Derivatives in Mice**
F. L. Rose and A. Spinks. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] **2**, 65–78, June, 1947. 1 fig., 17 refs.

The blood concentrations, following oral administration to mice, of a number of derivatives of sulphaguanidine have been determined, and the results analysed in the light of the hypothesis that the poor absorption from the gut of the parent compound is associated with structural features which may permit this substance to exhibit hydrogen bond phenomena. While much of the experimental evidence circumstantially supports this view, some of the results are inconclusive.—[Authors' summary.]

TOXICOLOGY

1951. **Sodium Nitrate Poisoning.** (Forgiftning med Natriumnitrat)
P. Amundsen. *Nordisk Medicin* [*Nord. Med.*] **34**, 1107–1111, May 9, 1947. 3 figs., 35 refs.

Fifteen persons were taken ill one evening after having eaten at 1.0 p.m. some cabbage prepared with sodium nitrate instead of cooking salt. Six died within 2 hours, 3 more on the way to hospital, and 1 immediately after admission. The survivors' most prominent symptom was cyanosis, particularly of the face, hands, and ears but in some cases of the whole body. The most severely affected patients also vomited. In 2 cases the vomiting was followed by convulsions, succeeded by coma and death within 2 hours. Administration of oxygen did not appear to relieve the condition in any way. Post-mortem examination showed that the blood was thick and chocolate-brown in colour and contained methaemoglobin; the cerebrospinal fluid was light brown in colour; the spleen was enlarged and congested; the liver was slightly enlarged and the kidneys showed moderate nephrosis and occasional corpuscular casts. Another patient died on the fifth day after an incompatible blood transfusion followed by renal failure, which was not relieved by decapsulation. Post-mortem examination revealed degenerative changes in the liver and circulatory disturbances in the brain. The 2 patients who recovered had dark serum and urine for some days; methaemoglobin [methaemalbumin ?] was found in the former; the urine contained blood and albumin. Both patients were discharged on the seventh day.

Discussing the action of the nitrate solution, the author suggests that the reduction of nitrate to nitrite by the bacteria of the gut was facilitated by the presence of carbohydrate from the large quantity of cabbage consumed, and that the symptoms observed were those of nitrite poisoning, the long latent period after the meal being due to the gradual reduction in the alimentary canal. Diagnosis of nitrite poisoning should be based upon cyanosis and the presence of methaemoglobin in the blood, and should be confirmed by tests for nitrates and nitrites in stomach washings and urine. Treatment consists of stomach wash-outs and administration of laxatives. *B. Nordin*

1952. **Pulmonary Edema and Pleural Effusion Produced by Acute Alphanaphthyl Thiourea Poisoning in Rats and Dogs**
H. Latta. *Bulletin of the Johns Hopkins Hospital* [*Bull. Johns Hopk. Hosp.*] **80**, 181–197, April, 1947. 8 figs., 14 refs.

Alpha-naphthyl thiourea (ANTU) is effective in the destruction of rodents by virtue of its high toxicity and good acceptability.

Five male and 12 female adult wild Norway rats injected intraperitoneally with 33 mg. ANTU per kilo were killed after 1 to 22 hours and major organs were studied histologically. Lesions were found only in the lungs, which showed oedema and pleural effusion, most

marked in animals allowed to survive longest. Perivascular oedema was first observed, then alveolar oedema, and finally filling of the alveoli with fluid which then extended to bronchi. Four estimates of protein in the fluid gave 3·6 to 3·7 g. per 100 ml. with plasma proteins 4·6 to 5 g. per 100 ml.; the fluid clotted and contained 360 to 1,400 leucocytes per c.mm. In a further 10 domestic Norway albino rats given 300 mg. per kilo orally and killed after 0·5 to 6 hours, oedema developed more rapidly in the lung than in the mediastinum.

Nine dogs were similarly studied. The pulmonary oedema was essentially similar to that seen in rats. The lymph flow in the cannulated right lymphatic duct of a dog given 20 mg. per kilo intravenously increased thirty-fold in 8 hours, at which stage the alveoli, bronchi, and pleural cavity filled with the excess. The experiments of Bing show cardiovascular changes to be secondary to fluid loss in lungs and pleural cavities. No myocardial changes were seen. Since increased pressure in pulmonary capillaries does not by itself result in pulmonary oedema it is concluded that ANTU increases pulmonary capillary permeability, death being due to anoxia. *George Brownlee*

1953. **Influence of 2,3-Dimercaptopropanol (BAL) on Blood Coagulation**
P. FANTL and M. H. NANCE. *Nature* [*Nature, Lond.*] **159**, 777–778, June 7, 1947. 1 fig., 13 refs.

Substances, such as cysteine, containing —SH groups affect blood coagulation. BAL markedly increases the prothrombin time, estimated by Quick's method. This has been shown to be due to actual inactivation of prothrombin, possibly by converting —S—S— groups to —SH radicles. BAL also reduces thrombin activity, but about 30 to 40 times the concentration is needed and the effect is not specific. Nevertheless, no change in blood coagulation or prothrombin time could be detected in rabbits given doses analogous to those used for the treatment of metal poisoning in man. It does not appear likely that BAL will produce haemorrhagic syndromes in man, in spite of its *in vitro* effect on blood. *M. C. G. Israëls*

1954. **Effect of Protein and Carbohydrate Intake on Liver Injury Produced in Dogs by Carbon Tetrachloride**
V. A. DRILL, T. A. LOOMIS, and J. BELFORD. *Journal of Industrial Hygiene and Toxicology* [*J. industr. Hyg.*] **29**, 180–184, May, 1947. 2 figs., 22 refs.

It has been reported that chlorinated hydrocarbons such as chloroform, ethylene dichloride, and propylene dichloride produce less hepatic injury when the diet is high in protein and low in carbohydrate than when it is low in protein and high in carbohydrate. This leads to the conclusion that the high-protein diet exerts a protective action. However, with carbon tetrachloride less hepatic injury was observed with a low-protein and high-carbohydrate diet than with the reverse, which suggests that a high-carbohydrate diet exerted a greater protection against liver damage than a high-protein diet. A similar protective effect of a diet low in protein but high in carbohydrate was observed in rats made to inhale carbon tetrachloride vapour.

In a first experiment 6 dogs were given for 6 weeks a normal diet containing 20% of casein. Then 3 of the animals were placed on the low-protein diet (8% casein) for 3½ weeks, the other 3 continuing on the 20% casein diet. At the end of the 3½ weeks 0·125 ml. of carbon tetrachloride per kilo was administered (by stomach tube with an equal quantity of corn oil) on days 1, 3, 5, and 7 of the investigation, while hepatic function was studied on days 3, 5, 7, and 9 by the bromsulphalein test. Only on the fifth day did both groups of dogs show similar changes in dye retention; on the subsequent days all the dogs receiving the low-casein diet showed less dye retention than those on the high-casein diet. The second experiment was similar, except that with the administration of carbon tetrachloride each dog received a daily supplement of 2 g. of methionine with the food. The results were as before. In the third experiment 6 dogs were kept on the 20% casein diet for 9 weeks, after which 3 of them were transferred to the 8% casein diet for 6 weeks, the other 3 still remaining on the 20% diet. Carbon tetrachloride was administered every other day for five doses; after this the dogs on low-protein diet showed normal dye excretion, whereas 2 out of the 3 dogs on the high-protein diet showed bromsulphalein retention. These series of observations therefore indicate that the diet low in protein and high in carbohydrate gave the better protection against carbon tetrachloride. Fatty changes in the liver were not significant in the two groups of dogs; necrosis was not observed in 6 of the animals fed on the low-protein diet but was present in 3 of the 6 dogs fed on high-protein diet. *H. M. Vernon*

1955. **Action of Mustard Gas (*ββ'*-Dichlorodiethylsulphide) on Nucleoproteins**
I. BERENBLUM and R. SCHOENTAL. *Nature* [*Nature*] **159**, 727–729, May 31, 1947. 15 refs.

Crude aqueous extracts of rabbit skin treated with mustard gas gave bulky protein precipitates which were shown to be due to a combination between mustard gas and nucleoprotein. Purified nucleoprotein was prepared from finely minced skin or thymus tissue by a series of extractions with distilled water, dilute borate buffer at *p*H 8·5, dilute acetic acid, and 0·05 N ammonia. The clear filtrate was desiccated by lyophilic drying and the powder extracted with light petroleum. This powder readily dissolved in alkaline solutions at and above *p*H 7·5. Acidification of the alkaline solution to below *p*H 6·5 resulted in precipitation of the protein. The powdered preparation contained 12·2% nitrogen, 0·89% phosphorus, and 1·1% sulphur; its relatively high ash content accounts for the low nitrogen value.

In standardized tests 0·5 to 1% nucleoprotein solution in M/20 to M/4 borate buffer at *p*H 9·0 was continually shaken with 1% mustard gas per volume of solution at 37° C. The *p*H of the solution was continually adjusted with dilute sodium hydroxide. Precipitation began within 2 to 5 minutes and was maximal in borate buffer at *p*H 8·5 to 9·0. Only slight precipitation occurred in

phosphate buffer between *p*H 8·0 and 9·0. Irreversible precipitation occurred in acetate buffer from *p*H 6·5 downwards. The poor precipitation in phosphate buffer was traced to the relatively high competition factor of phosphate ions for mustard gas. The precipitate produced by acidification of the alkaline nucleoprotein solution redissolved on addition of alkali, unlike the precipitate from mustard gas. The acid produced at the actual point of liberation was insufficient to account for the denaturation of the protein.

In standard tests lasting 20 minutes mustard gas did not produce precipitation in solutions of serum globulin, serum albumin, fibrinogen, prothrombin, gelatin, pepsin, or ribonuclease; haemoglobin gave a non-specific precipitation. In more rigorous tests slight turbidity was observed with pepsin, gelatin, albumin, and fibrinogen. The last reaction was non-specific. Greater precipitation was obtained with globulin under these conditions. The amount of nucleoprotein extractable from rabbit skin was greatly reduced or nil after treatment with pure mustard gas *in vivo* before extraction. Small amounts of dilute alcoholic solution of mustard gas applied to rat skin had little effect under similar conditions. A few compounds closely related to mustard gas similarly precipitated nucleoproteins, but lewisite gave no precipitation. Although $\beta\beta'$-dichlorodiethylsulphone and divinylsulphone produced no immediate precipitate, subsequent acidification of treated nucleoprotein solutions gave irreversible precipitation. The biological significance of the results is briefly discussed.

A. K. Powell

1956. **Treatment of Visual Disturbances due to Arsenical Trypanocides by Intravenous "Novocain" Injections.** (Essai de traitement par la novocaïne intraveineuse des troubles visuels causés par les arsenicaux trypanocides) H. Lorofi. *Presse Médicale* [*Pr. méd.*] **55**, 435, June 28, 1947.

Observations were made on 11 patients treated with arsenical preparations (tryparsamide and "orsanine") for trypanosomiasis. All patients showed varying symptoms of visual disturbance caused by these drugs. "Novocain", besides being an anaesthetic compound, when injected intravenously acts on the autonomic nervous system. Since the eyes are largely innervated by the autonomic nervous system, the use of novocain was tried in these cases of visual disturbance. The results were good, since 7 patients showed marked improvement, where there was complete amaurosis, and 2 partial improvement; in only 2 cases was there no improvement.

R. Wien

1957. **Pharmacology of Phosgene**
E. R. Trethewie. *Medical Journal of Australia* [*Med. J. Austr.*] **1**, 612–618, May 17, 1947. 6 figs., 12 refs.

Using the isolated lung and jejunum of the guinea-pig as test organs, the author shows that phosgene in small amounts liberates histamine and the "slow-reacting substance" of Feldberg and Kellaway from perfused organs, and suggests that histamine is mainly responsible for the pulmonary oedema characteristic of phosgene poisoning. [The technical details of this elaborate investigation do not lend themselves to a summary.] On this assumption thymoxyethyldiethylamine hydrochloride, a specific inhibitor of histamine, was administered 15 to 24 minutes after exposure of living guinea-pigs to fatal concentrations of phosgene started. A subcutaneous dose of 80 mg. per kilo body weight lowered the mortality rate from 88 to 38% in a group of 32 animals, half of which were treated and half used as controls. Unfortunately, small doses of thymoxyethyldiethylamine produce alarming symptoms in the human subject. [The abstracter, who has had a considerable experience of phosgene poisoning, recalls the more than encouraging preliminary results obtained with his colleague Harrison at Porton from the use of potassium salts and his disappointment after the experiment had been repeated several times; this kind of experience engenders a certain amount of suspicion about all favourable treatments for phosgene unless they are backed up by a very large number of trials.]

G. R. Cameron

1958. **Histamine and Phosgene Poisoning**
E. R. Trethewie. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 746–749, June 21, 1947. 2 figs., 8 refs.

Histamine is liberated by phosgene from the isolated perfused lung of the guinea-pig. The present paper is an extension of previous work concerning histamine liberation in the dog and the monkey. The lungs of the animals were perfused with Tyrode solution and ventilated with phosgene for 1 minute. Samples of the perfused fluid were tested for histamine activity on the isolated jejunum of the guinea-pig and for a capillary-damaging factor by intracutaneous injection in rabbits given trypan blue intravenously. In dogs an average of 63 μg. of histamine was liberated in 6 hours' perfusion after exposure; in guinea-pigs only 8 μg. was found in this time; in the monkey 211 μg. of histamine was liberated from the right lung during the same time. As the guinea-pig is very sensitive to histamine it is not surprising that it should be killed by a much lower concentration of phosgene.

In one experiment with a dead monkey histamine was found in the perfusion fluid before the lung was ventilated with phosgene. Immediately after exposure the histamine output increased twelve times, the fluid containing 4 μg. of histamine per ml. for 10 minutes. In the case of the live monkey given morphine and chloralose no histamine appeared in the sample before exposure to phosgene. Similarly, the lung of the dog given morphine and chloralose was perfused for 4 hours with Tyrode solution without histamine appearing in the fluid from the pulmonary vein.

To test for the presence of a capillary-damaging substance other than histamine, trypan blue (10 mg.) was injected into the ear vein of a rabbit and samples of the perfusion fluid were injected into the epilated skin. Dye did not pass out of the vessels into the skin with samples obtained before exposure to phosgene, but in most samples up to 60 minutes after exposure there was moderate activity in releasing dye. It is possible that

this new substance is identical with leucotaxine; its appearance is certainly evanescent.

Many experiments were carried out on treatment with varying doses of manganese, or ferrous sulphate, and vitamin C in mice and guinea-pigs, but the mortality rates were not lowered significantly. Iron and ascorbic acid break down histamine, but presumably the reaction is slow; manganese will afford some protection to guinea-pigs if it is given before induction of anaphylactic shock. The mortality rates among mice were slightly reduced by premedication with iron and ascorbic acid, but it would appear that a drug of the type of thymoxyethyl-diethylamine is required in the treatment of phosgene poisoning.

[It is not clear whether histamine was the substance estimated, since assays were completed only on the isolated guinea-pig jejunum and not confirmed by intravenous injections into cats. The animals received different doses of phosgene and these were not calculated on body weight, so it is difficult to compare results from different species. Lastly, the numbers of mice in each group used for prophylactic and therapeutic trials were quite small, in most experiments only 8.] *G. B. West*

INDUSTRIAL TOXICOLOGY

1959. **Acute Toxicity and General Systemic Actions of Diethylene Glycol Monoethyl Ether (Carbitol)**
P. J. HANZLIK, F. P. LUDUENA, W. S. LAWRENCE, and H. HANZLIK. *Journal of Industrial Hygiene and Toxicology* [*J. industr. Hyg.*] **29**, 190–195, May, 1947. 8 refs.

Diethyleneglycol monoethylether ("carbitol"), $CH_2OH.CH_2O.CH_2.CH_2O.C_2H_5$, is used extensively as an industrial solvent, in cosmetic products, and to some extent for external application as in vanishing creams and lotions. In the present investigation its action was determined by administering it in several ways to animals. The lethal dose (50% deaths in 48 hours) was found to be about 6 ml. per kilo in rats and mice when it was administered intragastrically, subcutaneously, or intravenously, but less than one-third of this amount when administered intraperitoneally to mice. For other animals it appeared to be more toxic, since the lethal dose (administered intravenously in dogs, cats, and rabbits and intragastrically in guinea-pigs) was about half that for rats and mice. Dilution with an equal quantity of water doubled the lethal dose, and this fact suggests that irritation was a factor in the higher toxicity of the undiluted agent. As regards ethylene glycol, the lethal dose varied considerably with the species of animal and the method of administration. Intragastrically in rats, mice, and guinea-pigs it was the same as, or higher than, that of carbitol, but subcutaneously in mice and intravenously in rats it was roughly one-half, and intravenously in rabbits about double. The lethal dose of diethylene glycol tended to be higher than that of carbitol and ethylene glycol. The approximate order of species susceptibility to carbitol and the ethylene glycols appeared to be: rabbit, dog, cat>guinea-pig>rat, mouse. Man is presumably more susceptible than the smaller rodents.

In most of the unanaesthetized animals used in this investigation symptoms were not demonstrable until more than 1 ml. of carbitol per kilo had been administered. Ataxia with an initial increase in respiration rate followed by a decrease occurred with doses of 2 to 2·5 ml., while depression, coma, and death resulted with 3 to 5 ml. There might be recovery in 1 or 2 hours from doses up to 2 ml., but with larger doses coma lasted 24 to 48 hours, generally without recovery. When the animals (dogs, cats) were anaesthetized with pentobarbitone the intravenous injection of carbitol caused an immediate but brief fall in blood pressure and slowing of the heart. Respiration was invariably depressed in both rate and amplitude; with the higher doses it stopped but returned with artificial respiration. *H. M. Vernon*

1960. **Tellurium. Accidental Exposure and Treatment with BAL in Oil.**
M. L. AMDUR. *Occupational Medicine* [*Occup. Med.*] **3**, 386–391, April, 1947. 14 refs.

Tellurium is a brittle silvery metal; in an alloy with lead, copper, and steel, it helps to prevent corrosion and mechanical and vibratory stress. It is also used in the chemical industry as a catalyst to convert heavy oils to motor fuels, and in the compounding of synthetic rubber; in ceramics it is used to produce yellow, green, and blue pigments. In bacteriology potassium tellurite is employed as a culture medium. In man the outstanding symptom of absorption is a persistent unpleasant garlic-like odour of the breath and the sweat due to the detoxification product, dimethyl telluride. Inhalation of the volatile hydrogen telluride experimentally has been accompanied by pulmonary irritation and haemolysis—massive intravascular destruction of the red cells with attendant jaundice, haemoglobinuria, and anuria. Three cases of tellurium exposure treated with BAL in oil are recorded. The men received injections of 2·5 mg. per kilo body weight intramuscularly into the buttock every 4 hours for 24 hours and every 6 hours for a second 24 hours, then one injection daily for 6 days. The first man reported the disappearance of the garlic odour in 14 days, the second in 11 days, and the third in 13 days. The short time within which this occurred suggests that tellurium may be added to the list of metals, poisoning with which has been successfully treated with BAL.
K. M. A. Perry

INSECTICIDES

1961. **Destruction of Adult Mosquitoes by Residual DDT Methods**
L. G. EDDEY. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. R. Soc. trop. Med. Hyg.*] **40**, 567–588, May, 1947. 8 figs., 1 ref.

The following is quoted from the author's summary: "In a series of preliminary trials conducted in large numbers of native dwelling-houses at Takoradi, Gold Coast Colony, it was found that a 1% solution of D.D.T. in kerosene, used to give a calculated deposit of 38·5 mg. D.D.T. per sq. ft. (929 sq. cm.) of room surface, produced

a marked relative absence of mosquitoes in the rooms treated. At the end of a 9-week check period following a single spraying the proportion between mosquitoes infesting the D.D.T. and control rooms had risen gradually to only 4 : 10. When the dosage was reduced to 11·9 mg. D.D.T. per sq. ft. the proportion 4 : 10 was reached in 13 days and complete parity with the control result ensued in a total of 28 days. No substantial lethal advantage was obtained by substituting the 'Maney' type sprayer for the 'knapsack' variety, and the latter was found to be the more efficient spraying apparatus for reasons given.

In a major trial conducted under semi-rural conditions in a non-malaria controlled area and using a dosage of 19·75 mg. D.D.T. per sq. ft., it was found that, despite its gradual increase, the D.D.T. index factor had still to attain to its initial level at the end of 9 months from the original date of spraying. Numbers of dead mosquitoes were collected in the treated rooms in the intervals between check sprayings throughout the first 10-week period.

Following adoption of the residual D.D.T. method as a routine in Takoradi township, and using a dosage of 19·3 mg. per sq. ft., sustained reductions in mosquito numbers were obtained over intervals of up to 18 weeks from dates of re-spraying. Further, the normal direct relationship ceased between rainfall and all species of mosquitoes collected, as also between rainfall and collected anopheline mosquitoes."

[This is an interesting paper; it does not lend itself to further summary and should be consulted in the original by those who are concerned for fuller discussion.]

R. M. Gordon

1962. **The Residual Action of DDT Against *Anopheles gambiae* and *funestus***
K. S. HOCKING. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. R. Soc. trop. Med. Hyg.*] **40**, 589–601, May, 1947. 2 refs.

The experiments described in this paper were carried out near Taveta in Kenya. Tents, huts, and wooden traps, all containing human " bait ", were used. Impregnations of 50, 100, and 200 mg. per sq. ft. (929 sq. cm.) of D.D.T. in kerosene were carried out with a power sprayer. A second tent was attached to the end of the first in an endeavour to ascertain the extent to which mosquitoes left a treated tent, the attached tents being referred to as " annexes ".

There is no interference with the normal behaviour of *Anopheles gambiae* and *A. funestus*, so far as entry into the huts and tents and biting of the occupants are concerned. When, however, the mosquitoes have been affected by contact with D.D.T. they tend to leave the building concerned, and as a result the number of mosquitoes in it is reduced. Thus, though there were much smaller numbers in the " unbaited " annexe than in the " baited " tent, the proportion in the annexe was much greater in the treated than in the untreated tent. It is concluded that " reduction in malaria transmission will not be achieved by mosquito mortality, however great, in a single impregnated building; to ensure this reduction similar treatment must be given to all human habitations in the neighbourhood, probably up to a radius at least as great as that found necessary in larval control of the anopheline species concerned. It cannot be expected that this method will be more than very partially effective as an anti-malarial measure against species which do not habitually rest in houses. Nor in a single house, or small group of houses, can this method be expected to be more effective than spray killing, although it is likely to be much cheaper . . . it seems . . . that the higher range of dosages used—namely, 150 to 200 mg. per sq. ft.—is necessary in order to achieve an adequate kill—that is, one in the region of totality. A necessary conclusion from the results given seems to be that, unless knock down is rapid, escapes will be considerable".

[The results are of considerable interest, particularly if they are compared with those recorded in Abstract 1961 and in Abstract 2246 in the section Infectious Diseases.]

R. M. Gordon

BLOOD TRANSFUSION

1963. **Nitrogen Balance and Blood Volume Studies in Man During and Following Repeated Plasma Transfusions**
F. L. MEYER, J. W. HIRSHFELD, W. E. ABBOTT, M. A. PILLING, H. H. WILLIAMS, and A. J. RICHARDS. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **213**, 160–169, Feb., 1947. 33 refs.

Few detailed studies of this type have hitherto been made in normal human beings. For this purpose the authors selected 3 male surgical patients convalescent from hernia or perforated peptic ulcer operations and of normal nutrition. Each patient was given a synthetic diet containing hydrolysed casein as the main source of protein, and nitrogen-balance estimations were made over a period of several days. All protein was then omitted from the diet for 5 days, on each of which a transfusion of plasma was given in an amount (1,000 to 1,480 ml.) calculated to contain the same quantity of protein as had previously been eaten daily. Following this, the synthetic diet was resumed during a period of further study.

A marked positive nitrogen balance (diminished urinary nitrogen excretion) was noted during the transfusion period. Thereafter urinary nitrogen excretion increased and a variable percentage (13%, 87%, and 50%) of the nitrogen gained was lost. Plasma volume was always increased by the transfusions but the increase varied inversely with the urine output. Haematocrit readings fell, partly as a result of blood dilution; in 2 cases, however, an absolute decrease in the circulating red-cell volume was noted. The total circulating protein in the plasma increased, but this increase, however, represented only about a quarter of the additional protein injected.

Full discussion of these and other phenomena will be found in the original paper by those interested.

Douglas H. Collins

Medical Jurisprudence

1964. **Signs of Absolute Death.** (Les signes de la mort absolue)
A. DANIEL and Mme A. DANIEL. *Avenir Médical* [*Avenir méd.*] **71–75**, Sept., 1946. 3 refs.

After recalling cases of revival of the apparently dead, the authors discuss the merits of various means of verifying that life is truly extinct. These include arteriotomy, cardiopuncture, and radiography of the heart; study of post-mortem changes in *p*H and of electrical conductivity and elasticity of fluids and tissues; the intravascular injection of fluorescein; and the use of Icard's thanatoscope and the hydrogen sulphide reaction. They stress the possible dangers of premature burial and urge the formation of an " Association contre le danger des inhumations prematurées ".

R. G. Bannerman

1965. **Rigor Mortis and Adenosinetriphosphate**
E. C. BATE-SMITH and J. R. BENDALL. *Journal of Physiology* [*J. Physiol.*] **106**, 177–185, June 2, 1947. 3 figs., 17 refs.

The authors, using rabbits as the experimental animals, noted that the onset and development of rigor mortis bore a direct relationship to the destruction of adenosinetriphosphate (A.T.P.). They suggest that the time of onset of the modulus and its rate of development depend upon the *p*H of the system and the prevailing rate of glycolysis. It is on these factors also that the destruction of A.T.P. depends. It is the destruction of A.T.P. alone, however, with which the onset of rigor mortis is associated, whether or not accompanied by glycolysis. As previously noted by Bate-Smith, animals which had been resting or narcotized before being killed exhibited a longer delay in the onset of rigor mortis than those which struggled violently or were killed immediately after other exertion. The present authors suggest two possibilities to account for these variations: (*a*) the fact that lactic acid is produced in the muscles as the result of struggling or exertion; and (*b*) a subsequent and sustained increase in the rate of glycolysis. They also found that shortening only occurred if the *p*H of the muscle was greater than 6·2 when stiffening set in. This *p*H, however, is apparently unusual in animals with a normal reserve of glucogen. *A. I. Suchecki*

1966. **A Note on the Causation of Sudden Death**
R. RICHARDS. *British Medical Journal* [*Brit. med. J.*] **2**, 51–53, July 12, 1947.

The author has analysed 1,694 cases of sudden, violent, or suspicious death examined for the procurator-fiscal. [The procurator-fiscal is the Scottish equivalent of the English coroner, and in most instances examines such cases by private inquiry rather than by inquest.]

In 823 cases the cause of death was definitely established in: (*a*) 527 cases subjected to necropsy (45 cases of neonatal death are omitted from the discussion), and (*b*) 296 cases of suicide not coming to necropsy because the cause of death was obvious from external examination. Of the 823 deaths, 200 were due to non-violent causes, 104 being accounted for by cardiovascular degeneration on which, in the majority of cases, was superimposed coronary atheroma and thrombosis. Infants are considered separately; 17 out of 24 died from diseases of the respiratory system. Of 599 deaths due to external agencies suicide was responsible for 365, coal-gas poisoning, drowning, and poisoning accounting for 83·6% of these.

Altogether necropsy was not performed in 1,122 cases, often because death occurred during the war years when such examinations were reduced to a minimum. There were 404 instances of sudden death in these 1,122 cases, and the author attributes 357 to cardiovascular causes. Of deaths due to external agencies 305 were caused mainly by injuries and drowning. Of the 105 deaths of infants in this group, 55 were due to respiratory causes.

The author points out that exact inferences cannot be drawn from the figures, but he stresses the predominance (76%) of cardiovascular disease as a cause of sudden death, and the frequency of coal-gas poisoning as a suicidal agent and of pneumonia as a cause of sudden death in infants.

P. N. Meenan

1967. **Sudden Deaths of Infants Allegedly Due to Mechanical Suffocation**
J. WERNE and I. GARROW. *American Journal of Public Health* [*Amer. J. publ. Hlth*] **37**, 675–687, June, 1947. 6 figs., 31 refs.

In the International List of Causes of Death, cause No. 182 is entitled " accidental mechanical suffocation ". In the U.S.A. in 1934, 834 deaths of infants under 1 year were classified under this heading; the number rose to 1,312 in 1944. One-half to one-third of all fatal accidents during infancy are attributed to this cause. During the past 15 years 167 consecutive cases of infants ordinarily certified under this heading have been investigated by the authors. In no case did they find that an infant had been suffocated. In 43 cases necropsy alone was sufficient to determine that death was due to a natural cause, mainly upper respiratory tract infection. In the remaining 124 cases histological study showed that fulminating respiratory disease was the most likely explanation for death in all except 15, in 6 of which no tissues were available for microscopical examination. An examination was also made of 67 other infants who had died suddenly in circumstances in which there could be no possible allegation of smothering. In these, acute respiratory disease was the usual cause of death, being present in 37 cases.

Analysis of the age incidence in notifications of suffocation shows that the peak occurs during the third and

fourth months, notification is infrequent in the first month when, if suffocation is the cause of death, one would expect to find the highest incidence. The relative freedom from death from infection in the first month may be explained by assuming: (1) that there is less exposure to infection, and (2) that the infant is still protected by maternal antibodies.

It is noted that the increase in notifications under No. 182 is accompanied by a decrease under No. 67 (disease of the thymus gland—mainly status lymphaticus) and No. 200 (undetermined causes of death). The view that a healthy baby will resist all attempts at suffocation is endorsed. The authors conclude that cause No. 182 is erroneous, and that efforts to prevent sudden death in infants should be directed towards diminishing exposure to infection and towards educating parents in the early signs of acute respiratory disease. *P. N. Meenan*

1968. **The Development from Known Methods of a Radiological Determination of Age by Study of the Proximal End of the Humerus.** (Entwicklung einer röntgenologischen Altersbestimmung am proximalen Humerusende aus den bisherigen Methoden)
H. BERNDT. *Zeitschrift für die Gesamte Innere Medizin* [*Z. ges. inn. Med.*] **2**, 122–128, Feb., 1947. 10 figs., 5 refs.

Examination of the proximal end of the humerus after maceration renders it possible to determine age, but this method has several disadvantages—the chief ones being the time consumed and the fact that disturbances due to the maceration itself may give rise to error. Radiological examination resulted in a considerable gain in time and accuracy and did not preclude further tests if necessary. Eighty-five humeri, from persons aged between 16 and 89 (some from exhumation cases), were used. Examinations were conducted on bones newly sawn open and washed and on bones sawn before and after maceration. All soft parts had been removed and the radiological examinations were carried out with 13 × 18 cm. plates at a distance of 70 cm. and with an exposure of 6·5 seconds.

A new criterion for age determination was found in a characteristic " pointed arch structure " of the diaphysis in the younger age group (17 to 26), which changes to a " columnar structure " at 30 to 40. This in turn becomes less definite or " interrupted " in the 40 to 60 age group, giving rise to a variable diaphysis formation and lack of determining signs. In the older person there is increased transparency with variable structure, proceeding later to absence of structure. *P. N. Meenan*

1969. **Cardiovascular Responses of Innocent Persons to Criminal Interrogation**
M. E. BITTERMAN and F. L. MARCUSE. *American Journal of Psychology* [*Amer. J. Psychol.*] **60**, 407–412, July, 1947. 1 fig., 4 refs.

Eighty-one university students, suspects in a case of theft but presumed innocent, were examined with the " lie detector " by the relevant-irrelevant method of interrogation. The polygraph records were studied by the two examiners working together, and it was found that although the respiratory tracings could not be classified easily the tracings for pulse rate, pulse amplitude, and blood pressure fell readily into the following categories: negligible reaction to all questions—31 records; non-differential response to all or nearly all the questions in one or more of the cardiovascular tracings, of moderate degree—23 records, and of extensive degree —20 records; differential response—that is, a more pronounced response to relevant than to irrelevant questions—7 records.

The records were classified also by a third person and by the two examiners independently about a week after the initial classification. A high degree of agreement between individual judgments and the initial combined judgments was found. The examiners regard the proportion of differential responses—that is, apparently incriminating reactions—by innocent persons as satisfactorily small, and state that the problem of " false positives " can be avoided by a more elaborate method of examination, the so-called " peak-of-tension " method. They conclude that the majority of suspects can be eliminated by a relatively brief test, if it is assumed that every guilty individual shows a differential response.
D. Russell Davis

1970. **Thermal Injuries Due to Electrical Accidents.** (Über Hitzeschäden nach elektrischen Unfällen)
F. JENNY. *Schweizerische Medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **77**, 780–782, July 19, 1947. 3 figs.

The author wishes to repudiate the statement that there is a difference between the changes in human tissues produced by electricity and those caused by heat.

The skin offers a resistance to the passage of electricity and, according to Joule's law, a part of this electrical energy is transformed into heat. Tissues damaged by heat and by electricity cannot be differentiated at histological examination. Similar changes have been described in cases of sepsis. Furthermore, bone splintering is not a characteristic feature of electrical injuries and is due to heat alone, as it occurs in the absence of muscular pull.

In order to prove his point, the author quotes three cases. In a case of severe electrical burns, especially of muscle tissue, the post-mortem findings and tissue histology were not unlike those seen in the crush syndrome. The second case was one in which destruction of the joint surfaces and elevation of the periosteum took place in an elbow-joint after severe thermal damage due to the passage of a high tension current. These changes are alleged to be due to an aseptic bone necrosis. In the third case destruction of the external table of the skull was caused by electro-thermal damage, with the formation of a rapidly fatal cerebral abscess.

Lumbar puncture in thermal injuries of the skull is only advisable if there is an increase in the production of cerebrospinal fluid; it is contraindicated if there is cerebral oedema.

[This article is convincingly illustrated by two radiographs and a reproduction of a sagittal section of the cerebral hemispheres.] *H. Jaslowitz*

Radiology

1971. **Progress in *X*-ray Stereoscopy.** (Fortschritte auf dem Gebiet der Röntgenstereoskopie)
I. LÜSCHER. *Deutsche Gesundheitswesen* [*Dtsch. GesundhWes.*] **2**, 27–29, Jan. 1, 1947. 2 figs., 1 ref.

The paper describes an apparatus for stereoscopic radioscopy. A self-rectifying circuit is used, and the two tubes are placed side-by-side, but with the cathode of one placed on the same side as the anode of the other. The tubes thus use alternately one half phase of the current. The image produced by each tube in succession is projected on a fluoroscopic screen. The observer uses a binocular which includes a vibrator. This vibrates synchronously with the A.C. current and covers up one visual field at a time, so that each eye receives the successive images projected by one tube only. In this way a true live stereoscopic picture is obtained. The binocular used by the author is the one described by Wiegelmann as the " Magneta stereoscopic binocular ". *A. Orley*

1972. **Absorption of Radon through the Skin and its Exhalation through the Lungs**
K. LANGE and R. D. EVANS. *Radiology* [*Radiology*] **48**, 514–516, May, 1947. 7 refs.

The range of the alpha rays from radon and its short-lived decay products is 30 to 50 μ, but one of the authors has observed lasting and deeply penetrating effects on the vascular structures of an area treated with ointments containing radon. There must, therefore, be diffusion of the radon in the ointment or absorption of the " lanoline " base by the tissues. Once present in the blood stream the radon should be transported to the lungs and permit a direct evaluation of the minimum quantity of radon absorbed from the ointment.

An ointment containing 44·4 microcuries of radon per ml. of lanoline was applied 2 to 3 mm. thick over an area of 25 sq. cm. to the leg of 4 patients in two experiments, and the amount of radon in the expired air was measured. Precautions were taken to avoid contamination of the room air and the inspiration of radon by the patients. In 1 case, the ointment was applied to a varicose ulcer. An appreciable amount of radon was recovered from the patients with intact skin, and still more from the one with the ulcer, amounting in this case in 23 hours to 10% of the amount applied. *A. G. C. Taylor*

1973. **The Early Effects of X-rays on the Ovaries of the Rat**
L. HALBERSTAEDTER and M. ICKOWICZ. *Radiology* [*Radiology*] **48**, 369–373, April, 1947. 6 figs., 9 refs.

The authors have set out to determine whether changes can be demonstrated in the ovary of the rat as early as 4 hours after irradiation by *x* rays. Doses varying from 50 to 2,000 roentgen units were used, on some rats to the abdomen only, on others to the head and thorax only, while others were totally irradiated. There were 4 non-irradiated controls. Serial sections of the ovaries were examined, the animal in each case having been killed 4 hours after irradiation.

In the follicles of the non-irradiated ovaries some pyknosis of the granular layer cells can usually be seen, but this is confined to follicles in which the ovum is in a state of division with the nucleus showing mitosis. Those with resting ova show very few pyknotic cells. In the irradiated series no difference was noted in the rats receiving 50 to 200 roentgen units. After a dose of 400 units and more, however, numerous pyknotic cells were observed in all follicles, both among the follicular cells and those in the granular layer. This appears to happen irrespective of the state of the ova. These findings applied only to the animals receiving direct abdominal irradiation or total irradiation. No abnormality was noted where the abdomen had been protected and the thorax only irradiated. Degenerative changes in the ovaries as early as 4 hours after irradiation, with doses exceeding 400 roentgen units, are thus demonstrated. Photomicrographs are given. *A. M. Rackow*

1974. **Lymphoblastoma. An Evaluation of the Differences in Sensitivity to X-ray Irradiation of Different Types, and Its Application to a Quantitative Therapeutic Test**
W. L. PALAZZO. *Radiology* [*Radiology*] **48**, 484–492, May, 1947. 3 figs., 14 refs.

The lymphocytic series is the most radiosensitive group of cells in the body; within it, the more immature cells —lymphoblasts and prolymphocytes—are the most sensitive. The author designates as lymphoblastomata the following conditions: (1) Giant follicular lymphadenopathy: generally benign but may undergo transformation into polymorphous-cell sarcoma, Hodgkin's disease, and leukaemia. This condition is extremely radiosensitive and may be cured by 300 to 1,200 r in fractions of 100 to 150 r. (2) Lymphatic leukaemia: as sensitive as the above, but nearly always fatal. (3) Lymphosarcoma: small-celled, large-celled, and reticulum-celled, can be kept in check for varying periods by one or two doses totalling 200 to 600 r. (4) Polymorphous-cell sarcoma: of doubtful origin; this may account for the fact that it is relatively radioresistant, doses of 1,300 to 2,500 r being required to cause regression or disappearance of involved lymph nodes. (5) Hodgkin's disease: the most refractory of all the lymphoblastomata to irradiation, but the dose required depends on the position of the nodes, varying from 1,000 r for superficial nodes up to 3,000 r for intrathoracic disease.

Irradiation is used as a therapeutic test in the diagnosis of mediastinal masses; 300 r is given on both the first and second days; if there is appreciable regression (25%

or more) by the fifth day a presumptive diagnosis of giant follicular lymphadenopathy or lymphosarcoma is made. If there is no regression, therapy is continued at the rate of 200 to 300 r daily, through anterior and posterior ports, and a presumptive diagnosis is made of polymorphous-cell sarcoma if the mass begins to show regression after 1,200 to 2,000 r. If 2,000 to 3,000 r is required to cause a 25 to 50% regression a presumptive diagnosis of Hodgkin's disease is made. If there is no response with 3,000 r, then the tumour is radio-insensitive, although substernal thyroid, enlarged thymus, thymic carcinoma, fibrosarcoma, melanosarcoma, oesophageal and bronchiogenic carcinoma, and sarcoid may show some degree of response to the higher dose. The doses are measured in air. Several ports are used for a mediastinal tumour. About 60% of radiation reaches it, so that a 3,000 r air dose should deliver about 1,800 r into the tumour. The radiation factors are 200 kV, 20 mA, a filter of 0·5 mm. copper plus 1 mm. aluminium, and a target-source distance of 50 cm.

[There is little evidence in this paper to support the views expressed. The method of expressing doses is confusing to the British reader, who may be left in doubt whether the doses delivered at the tumour have been known with sufficient accuracy to warrant some of the conclusions drawn.] *A. G. C. Taylor*

1975. **Roentgen Therapy in Hodgkin's Disease**
T. B. MERNER and K. W. STENSTROM. *Radiology* [*Radiology*] **48**, 355–368, April, 1947. 41 refs.

A series of 85 cases of Hodgkin's disease, proved by biopsy, has been reviewed in detail. Statistical evidence has been presented to indicate the multiple areas involved by Hodgkin's disease throughout the body. The peripheral lymph nodes are most frequently affected, followed by mediastinal nodes, abdominal nodes, spleen, and bones.

The disease is most common in the third decade and about two-thirds of the patients are males. A method of irradiation therapy has been developed at this clinic (University Hospitals, Minneapolis), which we believe is very efficient in the treatment of the lymphoblastomata. Treatment is considerably more intensive than in most series reported. A full course of therapy is applied to each area of involvement, the dosage varying between 1,000 and 2,000 tissue roentgens over a period of 14 days. Large masses are treated more intensely, and the group of enlarged nodes causing the greatest distress is treated first. Prophylactic irradiation, in our opinion, is contraindicated.

The 5-year survival rate from the time of treatment in our cases was 21% and the 10-year rate 8%, a high figure as compared with other series. Other statistics have also been presented, demonstrating the marked increase in the survival period from the onset of symptoms in treated cases as compared with a series of untreated cases of lymphoblastoma reported by Minot in 1926. The unpredictable nature of Hodgkin's disease is recognized and claims of cure cannot be made. Roentgen therapy has, however, markedly increased the survival rate.—[Authors' summary.]

1976. **Amebiasis. A Roentgen Study of Relatively Early Gastrointestinal Findings**
P. J. HODES and L. MAMMOSER. *American Journal of Roentgenology and Radium Therapy* [*Amer. J. Roentgenol.*] **57**, 329–332, March, 1947. 4 figs.

An account is given of the radiological findings in the intestinal tract occurring early in amoebiasis. Ninety-two patients, 60 of whom had no symptoms but passed cysts and 32 of whom had amoebic dysentery, were examined, 39 by barium studies of the small intestine and 92 by barium enemata. The small intestine examinations were carried out in the morning, the patients having fasted for at least 10 hours. The contrast medium consisted of 5 oz. (142 ml.) of barium sulphate suspended in 5 oz. of distilled water. The patients were examined at half-hourly intervals for the first 2 hours and every hour thereafter until the meal had appeared in the caecum. The usual technique was employed for barium enema examinations, except that routine air insufflation of the colon was not practised, as the work was done under field conditions.

Of the 32 patients with amoebic dysentery, 28 revealed abnormalities in the small intestine; 7 of the patients who passed cysts but had no symptoms were also examined, and in all but 1 the small intestine was normal. The most constant finding was rapid passage of the contrast medium through the small intestine, the oesophagus, stomach, and duodenum being normal. The small intestinal pattern on the whole was normal, but occasionally increased tone and bolus formation were present, this latter being particularly noticeable in the occasional patient who had hookworm disease in addition to amoebiasis. In a few individuals, decreased tone was associated with dilation of small intestine loops. Not infrequently the oral meal revealed an irritable, non-retentive caecum which looked normal on barium enema examination.

Of the 60 asymptomatic patients, only 10 showed minor abnormalities in the large intestine which seemed significant on examination by barium enema; these changes included increased tone and irritability of portions of the colon. Of the 32 patients with amoebic dysentery, 7 revealed irritability of the caecum; in 25 (79%) the results of barium enema examination were normal, even though the patients were passing pus and blood and ulcers had been seen with the proctoscope. It is possible that, had the double contrast technique been used, significant mucosal changes might have been observed. The authors suggest that examination by follow-through of a barium meal is of greater value than the examination by barium enema. *L. G. Blair*

1977. **Radiological Changes in the Colon in Amoebiasis.** (Alteraciones radiológicas del colon en la amebiasis)
C. JOSE NUNEZ and D. E. PALAZZO. *Medicina* [*Medicina, B. Aires*] **7**, 129–151, April, 1947. 19 figs., 13 refs.

The authors comment on the relative lack of literature on the radiology of the colon in amoebiasis. They quote Bell and Golden, who consider radiology valuable in the diagnosis of amoebic dysentery; the contrary view

is held by Manson-Bahr and Craig, the former regarding all ulcerative lesions in the colon as producing fairly similar pictures and the latter regarding radiology as of little value in the early stages but of some use in the later stages to determine the site and extent of the lesion.

This paper refers to the radiological investigations carried out on 8 patients, 7 men and 1 woman, between 19 and 70 years of age. All came from the region of Cordova. The first symptom was diarrhoea, and the histories showed that the duration had varied from 1½ to 8 years. Changes were found more often in the caecum and the ascending colon; in 2 cases the caecum was short, narrow, and tended to a conical shape. There were filling defects in the other parts of the large gut, but obstruction was never complete, even in a case in which there was a granuloma. It was impossible to decide whether the terminal ileum was affected structurally or just "functionally". The authors consider the following to be the salient features in the radiological picture: (1) The deformities occur most frequently in the caecum. (2) A normal intestinal pattern between the affected areas is common. (3) The caecum may show a conical shape at its lower border; this is attributed to a probable fibrous infiltration of the submucous and muscular layers during the reparative process. (4) The ileo-caecal valve is abnormally patent to the barium enema. (5) In view of the length of the histories, amoebiasis tends to produce less deformity than tuberculosis or ulcerative colitis.

There were no necropsies to correlate the radiological findings with any morbid changes. *Paul B. Woolley*

1978. **The Radiological Diagnosis of "Enteritis" and its Clinical Significance.** (Die Röntgendiagnose "Enteritis" und deren klinische Bedeutung)
H. Etter and J. Marti. *Radiologia Clinica* [*Radiolog. clin., Basel*] **16**, 181–192, May, 1947. 5 figs., 11 refs.

In the German radiological literature the commonly accepted signs of enteritis are: loss of the normal sharp herring-bone pattern, which is either blurred or replaced by indentations due to thickened or rigid folds; widening or narrowing of the intestinal lumen pointing to hyper- or hypo-tonicity; alternation of widened and narrowed segments suggesting loss of coordination and resulting in irregular filling; and changes due to hypersecretion. In order to demonstrate the reliability or otherwise of these signs, the authors examined the clinical notes of 139 cases in which the diagnosis of enteritis or irritation of the small intestine was made in the radiological institute of Berne University from 1937 to 1941. Their most interesting claim is that in all 48 cases where the final clinical diagnosis was enteritis, the severity of the case as judged by radiology agreed with the clinical picture. In the remaining 91 cases the *x*-ray findings need further explanation. There were 9 cases of infection—of the gall-bladder or appendix—where it seemed reasonable to suppose that the infection had spread to the gut. The 23 cases of peptic ulcer or peritonitis are also accepted as due to spread of the inflammation from the stomach downwards or from the peritoneum towards the gut lumen. Of 12 cases diagnosed as of "adhesions" it is noted that in 9 only disturbances of motility were shown by radiology. In 15 cases where there was an abdominal tumour, it is considered reasonable to suppose that the presence of the tumour favoured the development of a slight enteritis. In 6 out of 7 cases in which there was a disturbance of the circulation intestinal symptoms were absent, but it is thought possible that the *x*-ray findings were due to venous congestion or to irritation from the excretion of urea into the gut. In 11 cases diagnosed as of neurosis or psychopathy, the predominant *x*-ray disturbance was a change in tone. In the remaining 14 cases a variety of clinical diagnoses—such as constipation, thyrotoxicosis, tetany—were made, and in each case some theoretical justification for the *x*-ray picture could be advanced. The authors conclude that in most, if not in all, of their cases the *x*-ray finding contributes something to the pathological picture, though they believe that a distinction should be made between uncomplicated changes in motility and cases showing evidence of inflammation.

[The arguments are unacceptable to most British clinicians, who do not like to see the word "enteritis" used for disturbances of motility, secretion, and fluid content of the intestinal mucosa in cases where no definite abnormality can be detected under the microscope, and where there is little evidence that the dysfunction of the small intestine is important in the general clinical pictures.] *Denys Jennings*

1979. **Cholangiography and Biliary Regurgitation**
L. G. Rigler and H. W. Mixer. *Radiology* [*Radiology*] **48**, 463–471, May, 1947. 6 figs., 6 refs.

Cholangiography, the *x*-ray study of the biliary tract by direct introduction of a contrast medium such as "diodrast", may be accomplished at the time of surgical exploration; more commonly, the injection is made through a drainage tube post-operatively. Pre-operatively, the radio-opaque substance has been injected into a catheter placed in the gall-bladder through a simple abdominal incision and, more recently, with a needle thrust into the gall-bladder under the guidance of a peritoneoscope.

In a series of 460 cholangiographic studies the authors noted that in 8 cases the kidney pelves were clearly delineated by the dye. This renal excretion occurred within 15 to 30 minutes of the diodrast injection, but only in patients with a complete or partial obstruction of the common duct. This observation tends to establish the correctness of the theory that regurgitation into the blood stream of substances in the biliary tract may occur if sufficient pressure is exerted; in cholangiography care must be exercised to avoid the danger of forcing bacteria or other foreign material into the blood. *T. Semple*

1980. **The Physical Properties of Super-voltage X-rays.**
H. Miller. *Radiography* [*Radiography*] **13**, 37–41, April, 1947. 9 figs., 3 refs.

1981. **The Use of Isotopes in Medical Research**
J. H. Lawrence. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **134**, 219–225, May 17, 1947. 14 figs., 35 refs.

Pathology

1982. **Biochemical Studies During Malarial and Artificial Fevers**
E. A. GALL and A. STEINBERG. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **32**, 508–525, May, 1947. 2 figs., 50 refs.

Preliminary studies on 18 malarial patients had shown the development of a transient hypophosphataemia during febrile paroxysms. Serum phosphorus determinations were made during the rigor and at hourly intervals afterwards during sixteen febrile paroxysms in 12 patients with *Plasmodium vivax* malaria. In fifteen paroxysms the serum phosphorus level fell from about 3 mg. per 100 ml. to an average minimum value of 1·9 (1 to 2·9) mg. per 100 ml. within 1 to 3 hours of the onset of the rigor.

The behaviour during paroxysms of benign tertian malaria of a group of 17 patients, free from complicating diseases and injuries and not receiving any food or therapy during the experiment, was compared with that of a group of 7 fasting patients with minor eye ailments, subjected to artificial fever therapy in a fever cabinet at 104° F. (40° C.) (rectal) for 1·5 hours and 3 fasting patients with general paresis who were subjected to 106° F. (41·1° C.) (rectal) for 4 hours. Blood samples were collected and the temperature of each patient was taken regularly during a paroxysm. The blood samples were analysed by the copper-sulphate method for serum protein and spectrophotometrically for serum inorganic phosphorus, serum calcium, serum magnesium, serum potassium, blood glucose, and total blood-reducing substances. The blood from 2 malarial patients was examined for creatine and creatinine. The serum-phosphorus levels of the malarial and artificial-fever patients fell to average minimum values of 1·6 (0·8 to 2·7) and 2·3 (0·7 to 3·3) mg. per 100 ml. respectively. The blood-glucose levels of all the malarial and of most of the artificial-fever patients rose by about 50% and remained at high values after the temperatures had begun to fall. None of the patients exhibited glycosuria, and there were no significant changes in the calcium, magnesium, potassium, creatine, and creatinine levels. Some of the malarial but none of the artificial-fever patients showed a slight fall in serum-calcium levels.

The results are discussed, and it is suggested that hyperglycaemia is first produced by the accelerated metabolism during fever. Hexosephosphate is formed and deposited in the tissues, thus causing hypophosphataemia. At the end of the febrile episode, the hexosephosphate dissociates and the amount of inorganic phosphorus in the serum returns to normal.

J. E. Page

1983. **Arsenical Cancer: A Review**
O. NEUBAUER. *British Journal of Cancer* [*Brit. J. Cancer*] **1**, 193–251, June, 1947. Bibliography.

EXPERIMENTAL PATHOLOGY

1984. **Fluorescence of Cancerous and Non-cancerous Lipoids**
H. S. PENN and J. KAPLAN. *Nature* [*Nature, Lond.*] **160**, 18–19, July 5, 1947. 1 fig., 4 refs.

In a previous paper (*Nature*, 1942, **149**, 193) Penn produced evidence that human tumours contained a lipid fraction with a fluorescence spectrum very similar to that of methylcholanthrene. By contrast, corresponding fractions obtained from non-cancerous human livers showed a weaker fluorescence in a different region of the spectrum. Hieger (*Nature*, 1942, **149**, 300) disputed these findings, having failed to establish such differences in fluorescence between extracts of cancer and non-cancer tissues. Hieger's view was supported by Jones and May (*Cancer Res.*, 1944, **4**, 304), who obtained fluorescing fractions from the non-saponifiable lipids of human livers of both cancerous and non-cancerous origin, but with fluorescence spectra differing from those of polynuclear hydrocarbons.

The present paper describes a repetition, with technical modifications, of the original work and substantiates the earlier claim. The extraction processes and final separation of the components by chromatographic methods are outlined, and the fluorescence spectra of products from cancer and non-cancer tissues are illustrated and compared with fluorescence of methylcholanthrene. While noting slight differences between the spectrograms of the products of tissue origin and methylcholanthrene, the authors emphasize the similarity between them, but make no claim that the extracted component is identical with methylcholanthrene itself.

In an attempt to identify it chemically, they subjected the fluorescing fraction to hydrogenation but could detect no uptake of hydrogen; they conclude that the material consists largely of a saturated hydrocarbon, which could not be responsible for the observed fluorescence. The search for the fluorescing trace component is in hand.

H. G. Crabtree

1985. **The Species Character of Cancer Cells**
R. G. GREEN. *Science* [*Science*] **105**, 93, Jan. 24, 1947. 11 refs.

It is suggested that immunological studies on three mammalian tumours (mammary carcinoma of an inbred strain of mice, Shope papilloma, and Brown-Pearce cancer in rabbits) indicate that the species character of the cancer cell is not that of the animal of origin, but that of the associated virus. Intimate combination, or hybridization, of the virus with the animal cell changes its species character, causing it to grow neoplastically. A similar basic change may also be induced by carcinogens or radiant energy.

A. Haddow

1986. ***Trypanosoma cruzi* in the Treatment of Mouse Tumors**

T. HAUSCHKA, L. H. SAXE, and M. BLAIR. *Journal of the National Cancer Institute* [*J. nat. Cancer Inst.*] **7**, 189–197, Feb., 1947. 13 figs., 14 refs.

Relations between the rate of growth of tumours, course of infection with *Trypanosoma cruzi* or administration of trypanosome endotoxin, and alterations in the body weight of infected mice were studied.

The trypanosomes were cultured in Johnson's diphasic modification of Senekjie's medium (solid agar base, containing "bacto-beef", "neopeptone", and defibrinated rabbit blood, with a liquid overlay of Locke's solution). The *p*H of the medium was adjusted to 7·2 to 7·4. Subcultures were made at the peak of the logarithmic growth phase and no loss in virulence was observed. Mice were infected by intraperitoneal injections of 0·2 to 0·3 ml. of overlay from 2-weeks-old cultures, which averaged 82,000 organisms per c.mm. Although the trypanosomes grew less abundantly in Roskin's medium of citrated human blood and Ringer-Locke solution than in the modified Senekjie's medium, inoculations of both kinds of media were equally infective.

Endotoxin was prepared by storing overnight at 6° to 7° C. overlay from 2-weeks-old cultures grown in the modified Senekjie's medium, and subsequently heating the fluid for 30 minutes at 48° to 51° C. to kill the trypanosomes. This fluid was administered not later than 24 hours after its preparation and was injected intraperitoneally on 4 consecutive days in doses of 0·3, 0·3, 0·4, and 0·4 ml., respectively.

The transplantable tumours used were the squamous-cell carcinoma 119 in strain A mice, a mammary adenocarcinoma in C3H mice, and sarcoma 37 in mice of unknown genetic constitution. The spontaneous tumours studied were a mammary adenocarcinoma in female C3H mice and a breast tumour in female dba mice. Mice were infected by intraperitoneal inoculation of 0·2 to 0·3 ml. of fluid from 2-weeks-old cultures. Differences in tumour volumes of treated and untreated mice were used to evaluate the effects of endotoxin and infection with trypanosomes. The course of the infection was followed by counts of trypanosomes in thick blood smears. Smears were made every 10 days from the tail tips of all infected mice. A few mice in each series were killed at intervals for histological analysis.

The strain of *T. cruzi* studied was more virulent to A than to C3H mice. Infections reached a peak and blood populations of trypanosomes were maximal between 25 and 35 days after inoculation. Parasites were found in heart muscle, circular muscle of the small intestine, and connective tissue of the lung, but not in liver, spleen, brain, kidney, or ovary. Infected cells of carcinoma 119 were rarely seen, but leishmania forms were found in stroma and encapsulating connective tissue. No parasites were seen in the transplanted C3H tumours or in sarcoma 37.

The growth of the transplanted tumours, especially of sarcoma 37, was retarded by trypanosomiasis, but that of the spontaneous tumours was only slightly affected. The endotoxin was non-toxic to the mice, had no effect upon the growth of pieces of tumour soaked in it previous to implantation, and did not appreciably affect tumour growth when administered by intraperitoneal injection. Retardation of tumour growth by infection with the strain of *T. cruzi* used was attributed to non-specific factors and not to a direct action on tumour cells. Inhibition of tumour growth was often parallel by loss in body weight of infected mice and parasitization of vital organs. Differences in the strains of *T. cruzi* studied may account for the discrepancies between the effects of the trypanosomes on tumour growth observed in previous work and in the present investigations.

A. K. Powell

1987. **Bodily Reactions to Trauma. The Influence of Ischaemia on the Clotting Factor of Muscle**

H. B. STONER and H. N. GREEN. *British Journal of Experimental Pathology* [*Brit. J. exp. Path.*] **28**, 127–141, April, 1947. 4 figs., 38 refs.

Quastel and Racker (*Brit. J. exp. Path.*, 1941, **22**, 15) showed that ischaemia of various tissues increased the clot-promoting power of their saline extracts, and the present authors have further investigated this phenomenon in muscle extracts. They almost entirely occluded the blood supply of the hind limbs of rats with a special clamp, and made saline extracts of the ischaemic muscle and of the normal contralateral muscle. They measured the clot-promoting activity of the extracts by observing their power to accelerate the clotting time of recalcified oxalate plasma, and calculated the content of thromboplastic substance in the extracts by assuming a linear relationship between the logarithms of the concentration of the substance and of the clotting time.

The thromboplastic activity of muscle extracts rose rapidly with increasing periods of ischaemia, until a maximum threefold increase over the controls was reached after 4 to 6 hours' occlusion. The thromboplastic activity of muscle could not be increased by either aerobic or anaerobic incubation *in vitro*. The thromboplastic factor from ischaemic muscle was less thermolabile than that from normal muscle or brain, a property conferred by a dialysable constituent of the extract. Acetone extracts of muscle had less thromboplastic activity than saline extracts, and this difference was greater than the similar one between acetone and saline extracts of brain.

The clot-promoting substance in muscle extracts resembled thromboplastin in that it did not act in the absence of calcium ions, it did not clot pure fibrin, and its action on prothrombin-poor plasma was delayed. The increased activity of ischaemic muscle extracts was not due to contamination with blood, *p*H differences, or a better extraction of thromboplastin from damaged tissue. No trypsin-like enzymes or substances activating thromboplastin could be demonstrated in ischaemic muscle extracts. The authors conclude that ischaemia leads to the mobilization of thromboplastin stored in an inactive form in the cells, and suggest that this fact has a bearing on the general bodily reaction to trauma.

Martin Hynes

1988. **Heterologous Transplantation of Human Tumors**
M. E. SANO. *Science* [*Science*] **105**, 525, May 16, 1947.

Two human lymph-node tumours (questionable lymphosarcomata or leukaemias), after preliminary passage through tissue culture, were transplanted into mice. The lability of tumours difficult to diagnose is demonstrated by the varied types of tumour developing in the mice.

[Experimental details—such as the number of mice used—are not given.] *C. Waymouth*

1989. **Effects of an Antibiotic from *Aspergillus fumigatus* Fresenius on Tumor Cells *in vitro* and its Possible Identity with Gliotoxin**
J. G. KIDD. *Science* [*Science*] **105**, 511–513, May 16, 1947. 10 refs.

If tumour cells are briefly treated *in vitro* with filtrates of a strain (A21) of *Aspergillus fumigatus* Fresenius, the subsequent growth of tumours in susceptible hosts is inhibited. This effect has been demonstrated with 3 tumours: (1) Gardner lymphosarcoma of C3H mice; (2) a sarcoma (RSI); and (3) the Brown-Pearce carcinoma of rabbits. The tumour-inhibiting agent can be extracted with chloroform, is labile to heat in alkaline solution with loss of hydrogen sulphide, and stable to heat in acid solution. A crystalline material isolated from the A21 filtrate was indistinguishable from a sample of the antibiotic substance, gliotoxin, and purified gliotoxin was itself highly active against tumour cells. No effect visible through the ordinary or phase microscope was produced on the cells by the filtrates or the purified crystalline material. The aerobic and anaerobic glycolysis of tumour cells was not altered by doses more than sufficient to prevent subsequent growth. *In vivo*, intraperitoneal injections of filtrates or of the chloroform-extractable material do not significantly influence the growth of implanted tumours, but toxic materials distinct from the crystalline A21 substance and from gliotoxin are present. *In vivo* tests with the crystalline substances will be made when sufficient materials are available.
C. Waymouth

1990. **Anaphylactic Contraction of Human Smooth Muscle.** (Anafylaktická kontrakcia hladkého svalu u človeka)
L. DÉRER, O. LEHOŤAN, and A. HASIK. *Bratislavské Lekárske Listy* [*Bratislavské lekárs. List.*] **27**, 123–136, March, 1947. 17 figs., 21 refs.

The authors have studied the response to histamine, acetylcholine, arginine, and histidine, and to anaphylaxis, of the surviving human smooth muscle, removed at operation, in 83 strips from stomach, small gut, appendix, and gall-bladder. The smooth muscle was sensitive to acetylcholine in doses of 0·5 μg. per 100 g., but much less sensitive to histamine, the stomach requiring 200 μg. per 100 g., gall-bladder, jejunum, and ileum 60 μg. per 100 g., and appendix 10 μg. per 100 g. to produce a definite contraction. Histidine and arginine in 1/20, 1/40, and 1/100 molar concentrations showed inhibitory effects. The jejunum and appendix first showed an increase in tone and tonic contractions, but then a decrease in tone and complete refractoriness to histamine, and partially to acetylcholine, followed. However, simultaneous administration of histidine or arginine with histamine did not prevent histamine oedema or gastric secretion; on the contrary, the histamine effects were enhanced.

Twenty patients were sensitized before operation with 40 ml. of foreign serum. Muscles obtained at operation 10 to 28 days after sensitizing injection gave an anaphylactic contraction in only 3 of the 20 patients, though 12 patients had developed serum sickness and some of them had serum precipitins or positive skin tests. The 3 patients whose smooth muscles gave significant anaphylactic contractions were suffering from duodenal ulcer and all had had serum sickness about a week before; in none of them were serum precipitins demonstrable. The fact that an anaphylactic reaction of the surviving smooth muscle was obtained in only 15% of the "sensitized" patients is, in the authors' opinion, contrary to the view that smooth muscle plays a dominant part in the human anaphylactic reaction; it does not, however, rule out the importance of neuro-muscular complexes participating in the anaphylactic reaction *in vivo*. The apparent parallelism of the relative insensitivity to histamine and to serum anaphylactogen is stressed.
H. Pollak

CLINICAL PATHOLOGY

1991. **Comparative Erythrocyte Sedimentation Rates after Autohaemotherapy as a New Diagnostic Method.** (Die vergleichende Blutkörperchensenkungsgeschwindigkeit nach Eigenblutinjektionen als neues diagnostisches Hilfsmittel)
W. RUGE. *Schweizerische Medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **77**, 480–484, April 26, 1947.

The erythrocyte sedimentation rate (E.S.R.) was determined by Westergren's technique before, and 24 hours after, intradermal and intramuscular injections of the patient's blood. The E.S.R. was recorded as "mean sedimentation rate" (M.S.R.). If the 1- and 2-hour readings were a and b, then M.S.R.$=\frac{1}{2}(a+b/2)$. In normal untreated individuals this varied spontaneously by less than 20%, but in women it increased by 30% during the premenstrual period.

In 73·1% of 130 normal subjects autohaemotherapy appeared to have no effect on the M.S.R.; in 18·4% the M.S.R. increased by more than 30%, but repeated clinical examination showed either some focal infection or the early stages of an acute infection; in the remaining 8·5% the M.S.R. increased for no apparent reason. In patients with acute infections autohaemotherapy was followed by increases in M.S.R. of as much as 300%, but during early convalescence the M.S.R. fell to as little as 50% of its initial value. Patients with subclinical focal infections —for example, of teeth, tonsils, or prostate—showed marked increases after autohaemotherapy.

The author concludes that autohaemotherapy increases endothelial permeability and permits rapid attainment of

equilibrium between blood and tissue colloids. He recognizes three phases of infection: (1) onset or invasion, with high tissue and low blood colloids; (2) fastigium, or equilibrium; and (3) recovery, with high blood and low tissue colloids. Autohaemotherapy facilitates equilibration, and so is followed by increase in M.S.R. during phase 1, by no change in M.S.R. in phase 2, and by a decrease in M.S.R. in phase 3.

G. Discombe

1992. **The Erythrocyte Sedimentation Rate in Typhus Fever.** (Odezyn Biernackiego w durze plasmistym)
J. MAY. *Polski Tygodnik Lekarski* [*Polsk. Tyg. lek.*] **2**, 421–425, April 8, 1947. 1 fig., 4 refs.

The occurrence of typhus epidemics in Poland during the war enabled the author to study the erythrocyte sedimentation rate (E.S.R.) in almost 600 cases. These investigations were carried out in hospitals and field units; no precise statistical data could be collected. Westergren's method was used and the results were read after 1 hour.

All the cases were divided into four groups. The first group comprised cases of typhus without complications. The E.S.R. was found to be within normal limits or slightly increased (20 to 30 mm. in 1 hour) during the early febrile stage of the illness. The crisis was, however, regularly accompanied by a sharp increase in E.S.R., which continued to rise for the next few days. In the majority of cases the rise lasted for several afebrile weeks, decreasing gradually. In the second group, cases with lung complications, bronchopneumonia usually appeared about the time of the crisis and the E.S.R. increased sharply as in the first group. When bronchopneumonia occurred during the first week the E.S.R. rose early. In cases with meningeal and cerebral signs—the third group—the E.S.R. was not affected by their appearance. The fourth group consisted of patients with septic complications—such as abscesses, furunculosis, and bedsores. In all these cases the E.S.R. rose sharply. When septic complications appeared in the later stage of typhus the decrease in the E.S.R. was interrupted and a new increase was noticed, in some cases preceding the appearance of clinical signs. The author points out that only regular serial estimations of the E.S.R. are of any value in typhus fever. Although of limited diagnostic help it enables the course of the illness to be followed.

[This paper is followed by an editorial comment which criticizes the author's observations. His findings of a normal E.S.R. in the early stages of typhus cannot be conclusive, since the results were read after the first hour only.] *J. T. Leyberg*

1993. **On Plasma Lipids in Certain Internal Diseases.** [In English]
T. KALAJA and O. HELVE. *Annales Medicinae Internae Fenniae* [*Ann. Med. intern. fenn.*] **36**, 66–78, 1947. 14 refs.

Plasma cholesterol, cholesterol esters, and plasma phosphatides were determined in 15 normal subjects and 56 patients with various diseases. A table of the normal figures is given. No relation could be found between an increased erythrocyte sedimentation rate and the lipid content of the plasma. Among the patients there was a fall in lipid content in myeloid leukaemia, aplastic anaemia, pernicious anaemia, macrocytic anaemia, and liver disease. High values were found in subacute nephritis and in 2 cases of carcinoma of the head of the pancreas with secondary deposits in the liver. In patients with carcinoma no consistent alteration in values was found, and in diabetes mellitus the cholesterol rose out of proportion to the phosphatides. *Alan Kekwick*

1994. **A New Blood Sedimentation Technique: Inclined Tube Haemosedimetry.** (Une nouvelle technique de sédimentation sanguine: l'hémosédimétrie en tube incliné)
F. FUENTE-HITA. *Annales de Biologie Clinique* [*Ann. Biol. clin.*] **5**, 129–134, March–April, 1947. 10 refs.

1995. **Inclined Tube Blood Sedimentation. Clinical and Theoretical Interest of the Findings and their Relation to those in Vertical Tube Sedimentation.** (La sédimentation sanguine en tube incliné. Intérêt clinique et théorique de ses données et de leur relation avec les données de la sédimentation en tube vertical)
J. BADIN. *Annales de Biologie Clinique* [*Ann. Biol. clin.*] **5**, 135–149, March–April, 1947. 2 figs., 2 refs.

1996. **Effect of Various Blood Dilutions on the Rate of Globular Sedimentation in a Vertical and an Inclined Tube. Causes of the Phenomena Observed.** (Effets de diverses dilutions du sang sur la vitesse de sédimentation globulaire en tube vertical et en tube incliné. Causes des phénomenès observés)
J. BADIN. *Annales de Biologie Clinique* [*Ann. Biol. clin.*] **5**, 150–156, March–April, 1947. 6 refs.

It is alleged that there are two processes involved in blood sedimentation—namely, a descending current of corpuscles and an ascending one of plasma. If the tube is slanted, the corpuscles have a larger area over which to fall, while the ascending plasma does not have to percolate such narrow spaces between the falling red corpuscles.

The technique is, briefly, as follows: A 10-cm. column of blood in an 11-cm. tube, 5 mm. wide, is used in a stand in which it is inclined at an angle of 45 degrees. The diluting fluid is 3·7% sodium citrate mixed with the blood in the proportion of 1 to 5. By this method the reading, which would be reached in 1 hour by the vertical tube method, is attained in 15 minutes. For the male, figures in excess of 6 mm. in 15 minutes and 55 mm. when sedimentation is complete are regarded as pathological (8 and 55 mm. respectively for the female). The authors also pay attention to the details of appearance of the sedimented blood, using the method as a rather rough haematocrit method. The technique is not completely standardized. Fuente-Hita's method (mentioned above) is not the same as Badin's. The papers contain details of the results of using different dilutions of blood.

[Interesting though the results may be, there is insufficient evidence to support Badin's assertion that the Westergren method is an undeveloped stage of a potentially important haematological procedure.]

A. Piney

1997. **A Study of the Serum Biliverdin Concentration in Various Types of Jaundice**
E. A. LARSON, G. T. EVANS, and C. J. WATSON. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] 32, 481–488, May, 1947. 7 figs., 31 refs.

A description is given of a direct spectrophotometric method for the determination of biliverdin in serum or plasma, with records from 66 cases of jaundice. Significant values were obtained in 27 cases of carcinomatous obstruction of the common bile duct, 5 cases of stenosis of the common bile duct, 5 cases of cirrhosis, and 5 cases of infective hepatitis. No biliverdin was detected in the sera of 6 patients with transfusion reactions, or in 3 cases of haemolytic anaemia, although bilirubin was present. Serial observations were made on 12 patients, and in 3 cases biliverdin disappeared from the serum as the weight was increased by intensive feeding. A green tint was observed in the skin with values as low as 0·3 mg. per 100 ml. of biliverdin in the serum. *E. T. Ruston*

1998. **The Congo-red Test in Hepatic Diseases with Special Reference to Parenchymatous Icterus.** (Kongorotprobe bei Leberkrankheiten unter besonderer Berücksichtigung des Parenchymikterus)
J. SCHMID and W. WEISSEL. *Wiener Zeitschrift für Innere Medizin* [*Wien. Z. inn. Med.*] **28**, 237–246, June, 1947. 2 figs., 14 refs.

Fifty-four congo-red tests were carried out on 32 patients suffering from infective or obstructive jaundice or cirrhosis of the liver, some patients being subjected to one test only, others to three or four tests. The percentage of congo red disappearing from the serum was measured by an accurate colorimetric technique, a colour filter being used, in which the level of dye in the serum after 1 hour was compared with the level after 4 minutes. The results are given in a table together with the corresponding serum bilirubin levels; there is no doubt that as the serum bilirubin level rises the percentage of congo red disappearing falls.

Possible explanations of this inverse relationship are put forward and dismissed. The duodenum was intubated as a routine, the site of the tube being verified radiologically, and the authors feel justified in claiming that the late appearance of congo red in the duodenum in jaundice is only of secondary importance. In 5 patients, in whom a rigor followed the injection of old dye, the level of dye in the serum was actually greater after 1 hour than after 4 minutes. This is ascribed to loss of fluid from the blood with diminution in the circulating blood volume. There was no evidence that there was any comparable sudden fall in blood volume in the main series of jaundiced cases. A third explanation is given, which is believed to be the true one. A loose combination of serum protein with the dye is assumed to be an important stage in the removal of dye from the serum by the reticuloendothelial system. Evidence is cited that a loose bilirubin-protein compound diminishes the ability of the protein to adsorb congo red. The adsorption by cotton wool of dye from serum during 24 hours is compared with the rate at which dye vanishes during the normal test. A consistent relation emerges. In cases where the adsorption of dye by the cotton wool is greater than normal—so that less than the normal amount is adsorbed by the albumin—less than 25% of congo red vanishes from the serum in 1 hour. In cases where the adsorption of dye by the wool is less than normal, more than 25% vanishes in 1 hour. Exact technical details of the cotton-wool test are not given, but apparently each case had to be compared with a control to get over difficulties resulting from lack of standardized cotton wool.

[The authors agree with previous investigators that for a liver-function test, congo red is useless. The results do not parallel clinical estimates of severity or other function tests, and do not aid differentiation between obstructive and infective jaundice. The interest of the paper to British readers lies probably in its possible explanation of the anomalous results occasionally obtained in amyloid disease. If the authors' results are confirmed, it seems likely that a reduction in the vehicle function of the serum protein might to some extent counteract the absorption of dye by amyloid.]
Denys Jennings

1999. **Experimental Production of Anti-Rh Sera by the Use of Human Erythrocyte Stromata**
F. W. GALLAGHER and G. P. PILLISCHER. *Science* [*Science*] **105**, 344–345, March 28, 1947. 5 refs.

Rh-positive red cells were lysed with distilled water and the stromata washed until the supernatant fluid was free from haemoglobin. Guinea-pigs were "immunized by repeated intraperitoneal injection" of the residue. The guinea-pigs were subsequently bled and their sera were absorbed with Rh-negative red cells to remove the species agglutinins. Details are given of the reactions of two antisera produced in this way when tested against 109 samples of red cells which had previously been grouped with anti-Rh_0 [anti-D] serum. The results obtained with each guinea-pig serum agreed with the anti-Rh_0 results 103 times out of the 109. The two guinea-pig sera gave different results four times.

[Though it has possibilities from the point of view of research, the method is clearly unsuitable for the production of anti-Rh testing sera for routine purposes.]
R. R. Race

2000. **Serum Bilirubin and the Van Den Bergh Reaction**
C. GARDIKAS, J. E. KENCH, and J. F. WILKINSON. *Nature* [*Nature, Lond.*] **159**, 842, June 21, 1947. 6 refs.

No experimental evidence was obtained that the dual Van den Bergh reaction is due to the different strength of attachment of the pigment to protein. The differences in the type of reaction are due to the pigment itself, which is combined with serum albumin. Indirect bilirubin may be an intermediate precursor of bilirubin in the breakdown of haemoglobin. A direct-reacting serum will react as an indirect one after mild oxidation with 0·3% hydrogen peroxide, and the addition of pyridine (5%) to serum will change indirect to direct-reacting bilirubin. *E. T. Ruston*

Microbiology

2001. **Plasma Cellular Reaction and its Relation to the Formation of Antibodies *in vitro***
A. FAGRAEUS. *Nature* [*Nature, Lond.*] **159**, 499, April 12, 1947. 2 refs.

Rabbits were given a preliminary injection of a suspension of *Salmonella typhi* and were later given a secondary stimulus by a second injection of the same organism. During or after the rise in antibody titre (from 4 to 10 days after the secondary stimulus) pieces of tissue were removed from the animals and incubated in a mixture of rabbit serum, Tyrode solution, and sodium bicarbonate at 37° C. suitably aerated for 5 to 12 hours. The antibody in the splenic pulp mixture was of considerably higher titre than that in the lymph follicle mixture; that of the bone marrow and liver mixture was of still lower titre, and the thymus mixture contained no antibody.

[The antibody titres found were only of the order of one-thousandth of those in the serum of the animal at the time the experiment started, and it is not clear whether the antibody was produced *in vitro* as suggested or was washed out of the tissue during incubation.]

G. A. H. Buttle

BACTERIA

2002. **The Effects of Protein-Depletion and Subsequent Immunization Upon the Response of Animals to Pneumococcal Infection. I. Experiments with Rabbits. II. Experiments with Male Albino Rats**
R. W. WISSLER. *Journal of Infectious Diseases* [*J. infect. Dis.*] 80, 250–277, May–June, 1947. 12 figs., 52 refs.

Previous studies had shown a depression of the antibody-forming mechanism in animals suffering from a deficiency of protein in the diet. This report deals with the reaction of such animals to acute bacterial infection.

Rabbits fed on a diet deficient in protein and controls fed on normal diet were immunized by injections of a vaccine of pneumococcus type 1. The animals were later injected intradermally with a living culture; there was a significantly higher mortality rate among the rabbits on the poor diet. There was a correlation between the amount of antibody (measured as agglutinin) and resistance as measured by survival. Rabbits with a titre of 1 in 80 or less always developed septicaemia and died. The serum of rabbits on protein-poor diet was deficient in albumin. Immunization produced a greater increase in the serum globulin of normal rabbits than in that of the rabbits on special diet.

The results obtained in experiments with rats were similar to those obtained in rabbits, but deficiency of protein in the diet of the rat had the double effect of diminishing both the natural and acquired resistance to the pneumococcus. By means of mouse-protection tests a good correlation was demonstrated between agglutinin level and protective power of immune serum.

Histological examination of the skin lesions in different groups of rats showed that much of the phagocytic activity of the cells of normal rabbits was lost as a result of protein depletion. *Scott Thomson*

2003. **Isolation of Pleuropneumonia-like Organisms from the Bovine Genital Tract**
D. G. FF. EDWARD, J. L. HANCOCK, and S. L. HIGNETT. *Veterinary Record* [*Vet. Rec.*] **59**, 329–330, July 5, 1947. 11 refs.

Pleuropneumonia-like organisms have been isolated from the genital tracts of human beings with and without non-specific discharges. The authors, working at the Wellcome Veterinary Research Station, Frant, Sussex, now report the isolation of organisms of the pleuropneumonia group from the vagina of 18 out of 64 cows examined and from the semen of 6 bulls. The infected animals came from herds with long histories of breeding difficulties and showed evidence of inflammatory changes in the genital tract. *G. M. Findlay*

2004. **Studies on Staphylococcus Mutation: Characteristics of the "G" (Gonidial) Variant and Factors Concerned in its Production**
J. H. HALE. *British Journal of Experimental Pathology* [*Brit. J. exp. Path.*] **28**, 202–210, June, 1947. 4 figs., 14 refs.

Small colony "G" (gonidial) variants that remain stable after successive generations on nutrient agar plates were obtained by growth of staphylococcus in peptone water containing barium chloride and on nutrient agar plates containing gentian violet. This "G" form appears to be a discontinuous variant arising once in approximately 50,000 cocci. Its metabolic activities as estimated by growth rate and sugar fermentations are much lower than the parent strain. "G" variants have less resistance to heat and penicillin than the strains from which they are derived. The variant is feebly coagulase positive, but produces no α toxin. The possibility that the variant is nutritionally more exacting than the parent strain is discussed.—[Author's summary.]

2005. **Studies on Botulinum Toxoids, Types A and B III. Immunization of Man**
H. R. REAMES, P. J. KADULL, R. D. HOUSEWRIGHT, and J. B. WILSON. *Journal of Immunology* [*J. Immunol.*] **55**, 309–324, April, 1947. 7 figs., 12 refs.

Attempts to immunize man with fluid- and alum-precipitated (A.P.T.) *Clostridium botulinum* toxoid

showed that: (*a*) Four doses of toxoid at 2-week intervals gave the same result as three injections at 3- to 4-week intervals. The protective level of antitoxin (assumed to be 0·02 units of antitoxin per ml. serum) was reached only after the third injection, and not until the last dose of toxoid was given did 50% of sera from those immunized contain more than this amount. After four injections of toxoid given twice weekly 5 months after the start of the first course of injections 90% of those injected had over 0·02 unit per ml. serum; 30% had over 0·1 unit. "Booster" injections every 6 months are therefore recommended. (*b*) Three injections of A.P.T. at 3- to 4-week intervals gave a good response, the essential point being a long interval between the first and third injections. With mixed A.P.T. (A+B) two doses separated by 8 weeks gave a better result than two doses separated by 3 to 4 weeks. (*c*) Some persons injected did not respond at all. (*d*) Reactions are rare and moderate.

C. L. Oakley

2006. **Inhibition of Methionine Synthesis in *Escherichia coli* by 2-chloro-4-aminobenzoic Acid and Sulfanilamide**
F. B. Strandskov. *Journal of Bacteriology* [*J. Bact.*] **53**, 555–559, May, 1947. 5 refs.

A strain of *Bacterium coli*, resistant to the bacteriostatic action of 2-chloro-4-aminobenzoic acid (2-Cl-PAB) was obtained by culture of this organism in media containing varying concentrations of this substance. This 2-Cl-PAB-resistant strain, however, showed no greater resistance to sulphanilamide than did the parent strain. The addition of methionine renders both the parent and the 2-Cl-PAB-resistant strains more resistant to sulphanilamide, from which it is inferred that the sulphanilamide inhibits a process in the synthesis of methionine in addition to that inhibited by 2-Cl-PAB.

G. Payling Wright

2007. **Electron Microscope Studies of the "Interference Phenomenon" between Bacterial Viruses of the *Escherichia coli* Group**
M. B. Baylor and G. L. Clark. *Journal of Bacteriology* [*J. Bact.*] **53**, 49–55, Jan., 1947. 3 figs., 7 refs.

The virus interference phenomenon occurs with animal, plant, and bacterial viruses. It has been previously studied in respect of the latter (bacteriophages) by Delbrück and Luria, who have shown that infection of a *Bacterium coli* strain with phages T_α and T_γ (T_1 and T_2 of this paper) was followed by suppression of T_α even if it was added first; and that T_γ could still "interfere" even when inactivated by ultraviolet radiation (though with further radiation interference could also be abolished), a single γ-inactivated particle per bacterium being sufficient. They suggest that the effect is due to competition for an enzyme.

The authors obtained a visual demonstration of this interference by the use of the electron microscope. This was possible in view of the different morphology of the viruses. T_1 has a spherical head of uniform density 50 mμ in diameter; the tail is not well seen. T_2 has an oval head containing granules and a clearly observed tail. A series of electron micrographs showed: (1) Adsorption of the two viruses on the cell in approximately the numbers added. (2) Lysis of a cell with only T_2 in the cell debris. (3) Adsorption of large quantities of T_2 (following release and adsorption on adjacent cells) with some T_1 also. Titration of T_1 showed no increase. Titration of T_2 gave lower results than expected, and the "burst" size appeared smaller than indicated by the micrographs. It is suggested that clumping of the particles as seen in these may reduce titre, each clump acting as one particle on titration.

[The photomicrographs are not sufficiently clear to indicate properly the morphological differences described.]

G. T. L. Archer

2008. **Extraction and Determination of Small Quantities of Peptidase from Bacteria.** (Extraktion und Nachweis kleiner Peptidasenmengen aus Bakterien)
H. Bloch and E. Suter. *Schweizerische Zeitschrift für Pathologie und Bakteriologie* [*Schweiz. Z. Path. Bakt.*] **9**, 597–606, 1946. 3 figs., 14 refs.

The extraction of active enzymic preparations from bacteria necessitates the use of very large amounts of bacterial cultures. Experiments were undertaken to demonstrate that very active enzymic extracts can be obtained from a comparatively small volume of cultures by following the improved technique first elaborated by Zeller and Maritz. This method is based on the fact that all snake poisons examined by these workers were found to contain a very active *l*-amino-acid oxidase, reducing by oxidation the free amino-acids whereby one molecule of oxygen is used up for each molecule of the substrate. In the experiments recorded in this paper extracts were prepared from the Vallée strain of *Mycobacterium tuberculosis*, the "S.K." strain of *Bacterium coli*, *Staphylococcus aureus haemolyticus*, and pneumococci of undetermined origin; for the sake of comparison an extract made from the guinea-pig brain was also tested, and those extracts to which no snake poison had been added served as controls. The presence of peptidases was determined in as small quantities as 5 mg. per Warburg vessel. The extraction of dried bacteria ground with powdered glass furnished enzymic preparations which possessed, for quantitative determinations, a constant degree of activity. Such extracts proved to be extremely active in the case of such peptides as *l*-leucyl-glycine and *l*-leucyl-glycyl-glycine. In all extracts the presence of both di- and tri-peptidases was demonstrated, but the former were split more readily than the latter.

H. P. Fox

2009. **Conditions Contributing to Streptococcal Virulence. II. Intra-Phasic Attenuation by Sulfanilamide**
P. Hadley and V. Wetzel. *Journal of Bacteriology* [*J. Bact.*] **53**, 67–81, Jan., 1947. 7 refs.

Working with a somewhat atypical strain of α streptococcus, a detailed description of which is therefore given, the authors in a previous paper showed that the greater proportion of the increase of virulence observed during animal passage of the rough variant took place after

demonstrable roughness had disappeared. This was referred to as "intraphasic" variation in virulence. Using the same strain they now show that the development of sulphonamide resistance may be associated with a marked intraphasic fall in virulence.

Thirty-nine serial passages in increasing concentrations of sulphanilamide were made beginning with 5 at 1/10,000 dilution and ending with 15 at 1/100. A control series of broth passages was carried out, and observations were made of morphology, cultural characteristics, and mouse virulence (the latter after one further subculture in plain broth for both series to avoid injection of the drug with the inoculum in the test series). Inocula were checked by colony counts and, in some cases, by turbidity, since varying chain length affected the value of the count method. After four passages at 1/10,000 dilution virulence was considerably diminished, after thirteen passages (last three at 1/3,000) M.L.D. was about 1,000 times that for the control culture after thirty-nine passages (during which time the M.L.D. increased about ten times above its original level). Further passages in sulphanilamide produced only a slight further fall in virulence. The sulphanilamide concentrations were so graded that little bacteriostatic effect was produced. The strain remained in the smooth phase except for "a few brief excursions towards the rough" throughout the experiment, though growth in broth took the form of a flocculent deposit in place of diffuse clouding as the passages progressed. The control series continued to give a homogeneous growth. Virulence was not readily regained by reversion to more normal conditions, since seven further passages in blood broth after the thirteenth in sulphanilamide were without effect.

These results are discussed in comparison with reports on the failure to produce diminution of virulence of pneumococci *in vitro*, the loss of virulence of the same species associated with cultural "modulations" produced *in vivo*, and the mucoid smooth variation with loss of virulence produced on β haemolytic streptococcus *in vitro* by the action of sulphonamides. It is suggested that phasic transformation is more likely when the initial concentration is high and increases are rapid. As regards the intraphasic attenuation observed "whether this unusually broad range . . . is characteristic of greening streptococci in general or is limited to certain species remains . . . a question". *G. T. L. Archer*

2010. **Nucleotide Metabolism of Bacteria and the Bacterial Nucleus**

B. MALMGREN and C. G. HEDÉN. *Nature* [*Nature, Lond.*] **159**, 577–578, April 26, 1947. 1 fig.

A technique was employed which enabled the order of magnitude of the nucleotide content of bacteria to be determined by photometry of micrographs. Both Gram-negative and Gram-positive bacteria were studied (*Bacterium coli*, *Aerobacter aerogenes*, *Proteus vulgaris*, *Flavobacterium*, *Bacillus cereus*, *Staphylococcus albus*, *Streptococcus faecalis*, *Spirillum rubrum*, and *Corynebacterium diphtheriae*). In all cases during the early phase of bacterial growth there was considerable increase in nucleotide content, which reached its maximum during the end of the lag phase or the beginning of the logarithmic phase. The increase was five to ten times the initial content. On the basis of observations made by ultraviolet microspectrography, and by the Feulgen staining method, it is concluded that both ribose and ribodesose systems are involved in bacterial growth. A nuclear mechanism of the same functional type as that in metazoan cells is postulated, with two types of nucleotides. These constitute a functional unit, but are not combined functionally. Ribodesose organella which undergo fission correspond to the euchromatin of metazoan cells and induce the formation of gene proteins. The ribose nucleotides are functionally equivalent to heterochromatin and control the formation of the proteins of the cell body. *R. J. Ludford*

2011. **Use of Papain in Cultivation of Bacteria from the Blood**

F. DREYFUSS. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **17**, 365–371, May, 1947. 14 refs.

A papain-broth medium is recommended for blood cultures. The preparation of the medium is simple. A 2% saline suspension of the enzyme papain is filtered through paper, and after 24 hours is passed through a Seitz filter. The clear, yellow fluid can be kept for a fortnight in the refrigerator, and is added to plain or brain–heart infusion broth in sufficient quantity to make a 10% concentration. Papain-saline proved to be a nutrient medium in itself. It is claimed that it combines many of the advantages of saponin and trypsin; in the author's hands, it appeared to be useful in isolating streptococci, especially of the viridans type. The growth of micro-aerophilic organisms is also favoured. Papain-broth serves as an anticoagulant, is shown to inhibit action of sulphonamides and penicillin (the latter because of a contaminating subtiloid bacillus contained in the dry powder), and has complement-fixing properties, thereby enhancing the growth of organisms. Because of its fibrinolytic action it can be employed with advantage when clot cultures are to be made. *R. Salm*

2012. **Comparison of Various Methods of Preserving Stool Specimens containing Dysentery Bacilli.** (Сравнительная оценка различных консервирующих смесей при исследовании faeces на присутствие дизентерийных микробов)

N. Y. SILBER, M. R. NECHAEVSKAYA, and K. V. GONCHAROVA. Врачебное Дело [*Vrach. Delo*] **26**, 691–696, 1946.

Glycerin is commonly used for preserving the viability of dysentery bacilli in stool specimens which have to be transported before culture, but this method suffers from the disadvantage that some samples of glycerin may possess antibacterial activity. The authors have investigated other methods of preservation, and find that good results are obtained if the faeces are placed in either of the two following solutions: (1) saline containing 1 to 2 ml. 10% NaOH per litre; (2) distilled water with ammonia added to bring the *p*H to 7·8; after sterilization this usually contained 65 mg. ammonia per litre.

The efficacy of the method was tested in experiments in which stool specimens artificially infected with dysentery bacilli were placed in the two preservative solutions, and also in glycerin and saline for control purposes. Twelve experiments were carried out in each group; 100 million Flexner and Sonne bacilli were added, and the mixtures were kept at room temperature (18° C.). Sub-cultures were carried out at intervals from 2 to 72 hours. With the ammonia and alkali mixtures there was a definite prolongation of survival time as compared with the controls. The experiments were repeated with 10 and 1 million organisms, and similar results were obtained. Ammonia is presumed to act by inactivating bacteriophage. In one experiment a polyvalent phage was added to the mixtures; dysentery bacilli could be isolated up to 72 hours in the ammonia and alkali mixtures, but only up to 8 hours in the controls. Stool specimens from 79 cases of dysentery were examined by the method; 27 isolations were made with glycerin conservation, 31 with ammonia, and 34 with alkali mixtures. [The duration of conservation is not stated.] *D. J. Bauer*

PROTOZOA

2013. **The Nutrition of Protozoa. I. A Simplified Medium for the Investigation of Unknown Factors in Blood Serum Essential for the Sustained Growth of *Trichomonas vaginalis***
H. SPRINCE and A. B. KUPFERBERG. *Journal of Bacteriology* [*J. Bact.*] **53**, 435–439, April, 1947. 6 refs.

Most media suitable for the cultivation of parasitic protozoa contain blood serum, but very little is known about the growth factors for these organisms contained in serum. With a view to testing the effect of various fractions of serum upon the growth *in vitro* of *Trichomonas vaginalis*, the authors have devised a medium which can be prepared in a minimum of time, which is complete as regards serum or its fractions, and the composition of which is chemically well defined.

The composition of this medium, known as " trypticase nutrient medium " and representing a modification of Johnson and Trussell's medium, is as follows: trypticase 200 mg.; sodium acetate+$3H_2O$, 48 mg.; cysteine hydrochloride, 15 mg.; maltose, 10 mg.; " difco " agar, 10 mg.; $NaHCO_3$, 5 mg.; asparagine, 2 mg.; ascorbic acid, 1,000 μg.; choline chloride, 80 μg.; inositol, 80 μg.; ribose, 40 μg.; adenine sulphate, 40 μg.; guanine hydrochloride, 40 μg.; xanthine, 40 μg.; uracil, 40 μg.; riboflavine, 8 μg.; thiamine hydrochloride, 1·6 μg.; pyridoxine hydrochloride, 6·4 μg.; pyridoxamine hydrochloride, 1·6 μg.; pyridoxal hydrochloride, 1·6 μg.; calcium pantothenate, 3·2 μg.; nicotinic acid, 3·2 μg.; *p*-aminobenzoic acid, 1·6 μg.; biotin, 0·8 μg.; folic acid, 0·8 μg.; methylene blue (optional), 24 μg.; adjusted to *p*H 6·0 and with Ringer's solution added to make 8 ml.; to this is added 2 ml. of human blood serum diluted with an equal volume of Ringer's solution, giving a final volume of 10 ml. In this medium *T. vaginalis* has been grown readily through 60 transfers, producing mobile flagellates uniform in size and shape.

For the assay of serum fractions the intact serum in the medium is replaced by any given fraction or combination of fractions by adding 2 ml. of the material to be tested to 8 ml. of trypticase basal medium. When less than 2 ml. is used, Ringer's solution is added to compensate for the difference, since the final volume of each tube should be 10 ml. to permit a comparison of cell counts in the tests and intact serum controls.

C. A. Hoare

2014. **The Nutrition of Protozoa. II. The Separation of Human Blood Serum into Two Fractions, Both Essential for the Sustained Growth of *Trichomonas vaginalis***
H. SPRINCE and A. B. KUPFERBERG. *Journal of Bacteriology* [*J. Bact.*] **53**, 441–447, April, 1947. 8 refs.

Using the trypticase basal medium described in the previous paper (Abstract No. 2013) the authors tested the effect upon growth *in vitro* of *Trichomonas vaginalis* of two fractions of human serum. One of these is an ether-soluble fraction, the other the aqueous ether-insoluble residue left over after the extraction. Neither of these fractions alone is capable of supporting growth, but the addition of both provides a complete nutrient medium. One of the active components of the ether-soluble fraction is linoleic acid, while serum albumin is one of the active components of the aqueous ether-soluble fraction. Both fractions contain factors required to produce optimal growth of the trichomonad, but their nature has not yet been determined. *C. A. Hoare*

2015. **Studies on the Culture of *Endamoeba histolytica***
J. N. DELAMATER and F. A. HALLMAN. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **65**, 26–29, May, 1947. 3 refs.

A heat-stable (100° C. for 4 hours), dialysable substance has been demonstrated in the protein-free fraction of human serum. This substance is essential to the growth of NRS strain of *Endamoeba histolytica* in egg-white buffer infusion medium containing starch. Partially deproteinized filtrate of human serum diluted in an equal volume of M/15 buffer, with rice starch added, constitutes a simple medium for the propagation of *E. histolytica*. Rice starch appears to act as a temporary inhibitor to bacterial multiplication in these cultures. Such suppression leads to more satisfactory growth of the amoebae present. Study of the biology of the bacteria in these cultures may give further information concerning the complex metabolic requirements of *E. histolytica*.—[Authors' summary.]

2016. **Intradermal Reaction in Trichomonas Infection**
S. ADLER and A. SADOWSKY. *Lancet* [*Lancet*] **1**, 867–868, June 21, 1947.

2017. **Prolonged Storage of Human Pathogenic Protozoa with Conservation of Virulence: Observations on the Storage of Helminths and Leptospirae**
D. WEINMAN and J. MCALLISTER. *American Journal of Hygiene* [*Amer. J. Hyg.*] **45**, 102–121, Jan., 1947. 16 refs.

IMMUNITY

2018. **Pre- and Post-natal Development of Immunity. Serum-albumin and Serum-globulin Levels in Maternal and Cord Bloods of Premature Infants**
C. RIMINGTON and J. A. BICKFORD. *Lancet* [*Lancet*] **1**, 781–785, June 7, 1947. 2 figs., 35 refs.

To obtain information on serum protein levels of full-term and premature infants the total protein, non-protein nitrogen, albumin, and globulin were determined in the cord blood of 38 newborn children, whose conceptual age varied from 20 weeks to full term. Parallel determinations were made on maternal blood. Foetal albumin and globulin increase with length of gestation and at about the same rate. No significant change in maternal serum protein occurs during pregnancy, and there is little correlation between maternal and foetal values. It is suggested that a foetal method of synthesizing serum protein is in use in the early stages of gestation, and is later displaced by the adult method; this might explain the " serological immaturity " of the newborn.

Attention is drawn to the interest of the osmotic relations of foetal blood, with its low serum protein content. *C. L. Oakley*

2019. **Physiological and Immunochemical Reaction of Antigonadotrophic Sera.** (Activité physiologique et immunochimique des sérums antigonadotropes)
A. BUSSARD and P. GRABAR. *Bulletin de la Société de Chimie Biologique* [*Bull. Soc. Chim. biol.*] **29**, 195–211, Jan.–March, 1947. 27 refs.

Rabbits were injected on 4 consecutive days a week for 4 weeks with increasing doses of gonadotrophic hormone of varying purity; they were rested the remaining 3 days, and were bled by cardiac puncture at the end of the fourth week of immunization. The antigens used were either gonadotrophin solutions injected subcutaneously or preparations adsorbed on alumina injected intravenously. Sera obtained from these rabbits were tested *in vivo* and *in vitro* for their capacity to react with chorionic gonadotrophin, either when fresh or when adsorbed with human serum or human urinary proteins. *In vivo* tests were carried out by the injection of four doses of chorionic gonadotrophin into immature female rats at 24-hour intervals, each injection being preceded by the subcutaneous injection of the test serum. At 120 hours the rats (weighing not more than 55 g. at the end of the experiment) were killed and examined for: (1) opening of the vagina; (2) presence of haemorrhagic ovarian follicles; (3) ovarian weight per g. body weight; and (4) uterine weight per g. body weight. By all these tests the sera showed considerable antigonadotrophic activity even after absorption with human serum. If gonadotrophin and rabbit antiserum were mixed before injection, antigonadotrophic activity appeared lower than when the components were injected separately.

Antigonadotrophic sera precipitate readily on mixture with gonadotrophin, and the values so obtained agree fairly well with the *in vivo* values, even after precipitation with human serum. The amount of nitrogen precipitated is, however, far less than the amount of gonadotrophin neutralized would lead one to expect, suggesting (as is confirmed by other evidence) that the gonadotrophins used are extremely impure. Antigonadotrophic sera also give precipitates with some samples of pregnancy urine, though not with citrated urine. Pregnancy urine purified by treatment with saturated benzoic acid in acetone and subsequent concentration always gave a precipitate with antigonadotrophic sera (one control urine also gave a precipitate).

If antigonadotrophic sera and " pregnyl " (a commercial gonadotrophin preparation) are allowed to react, the washed centrifuged precipitate shows some gonadotrophic activity. The supernatant precipitated with both pregnyl and antigonadotrophic sera, suggesting that pregnyl contains more than one antigen. Treatment of the supernatant with 0·1 N sodium hydroxide had little effect on its gonadotrophic activity, while that of the precipitate was completely destroyed. Fractions treated with NaOH showed a correlation between the effects on vaginal opening and ovarian weight, but no correlation between these and uterine weight, supporting the view that impure chorionic gonadotrophin preparations contain more than one active substance.

C. L. Oakley

2020. **Immunization of Human Beings with Red Cell Eluate and other Types of Influenza Vaccine**
R. HARE, D. M. MACKENZIE, L. MCCLELLAND, and M. CURL. *British Journal of Experimental Pathology* [*Brit. J. exp. Path.*] **28**, 141–152, April, 1947. 3 figs., 11 refs.

The red cell eluate vaccine promises to give some protection against influenza A and B, but the usual dose of 1 ml. of a tenfold concentration of the material derived from two or three eggs is expensive. The authors made experiments to determine whether a smaller dose or a less concentrated vaccine would be equally efficacious. They used a commercially-produced influenza A and B red cell eluate vaccine, and vaccines in which the influenza A component had been concentrated by alum precipitation or by alternate freezing and thawing. They immunized groups of 20 human volunteers, and estimated the degree of immunity by titration of the serum by the red cell agglutination-inhibition method before, and at intervals after, the inoculations. The protection of mice against living intranasal vaccine was also tested.

About one-quarter of subjects receiving the undiluted vaccine had a febrile reaction, a quarter had " chills without fever ", and a quarter had local reactions only. The serum titres fell in the first few days after inoculation, but regained their former level after 1 week and rose to a maximum after 2 weeks. Some subjects did not respond to the vaccine, and the magnitude of the response in the others was very variable. Vaccine diluted with an equal volume of saline was only slightly less efficient than the undiluted material, but further dilution much reduced the response. The raised titre of antibody was unexpectedly maintained during the 16 weeks after inoculation, and a further rise was sometimes seen. The presence

of influenza A and B in the neighbourhood during the experiment was probably responsible for these phenomena.

Vaccines in which the influenza A component was concentrated by alum-precipitation or by alternate freezing and thawing had no advantages over the red cell eluate vaccine, but gave an immunogenic response in proportion to their virus content.

Experiments on mice indicated that the mouse antigenic test officially recommended in the U.S.A. for the testing of influenza vaccines is too lax a test of their immunizing ability in man.

The authors conclude: "The original allantoic fluid containing influenza virus must be concentrated 10 or 13·3 times, a full dose of 1 ml. of the concentrate should be given, a proportion of those receiving this dosage will suffer reactions, a negative phase will be produced, and if antigenic tests are employed as a measure of the potency of vaccines, they must be made considerably more stringent than those at present employed".

Martin Hynes

2021. **Histological and Serological Sequences in Experimental Hypersensitivity**

C. VAN Z. HAWN and C. A. JANEWAY. *Journal of Experimental Medicine* [*J. exp. Med.*] **85**, 571–590, June, 1947. 12 figs., 39 refs.

Groups of rabbits were injected intravenously with single large doses (1 g. per kilo body weight) of solutions of crystalline bovine serum albumin and bovine serum γ-globulin. A further group received crude bovine serum in volumes containing this amount of protein. Animals were killed in small groups at the end of 1 week and 2, 3, and 4 weeks, their sera tested for antigens and antibodies, and their tissues examined histologically for signs of injuries to arteries and other structures.

In the group injected with crystalline serum albumin several animals developed focal arterial lesions. In those killed early these took the form of leucocytic infiltrations in the vessel wall; in those killed later fibroblastic proliferation had taken place and minute granulomata had developed. In a few animals the endocardium showed similar changes. Tests for circulating antigen and antibody revealed that even at the end of 4 weeks the animals had some of the former in their plasma, but little, if any, of the latter.

The rabbits injected with bovine serum γ-globulin showed a high incidence of acute glomerulonephritis in those killed at the end of the first week. In those killed later no acute lesions and only varying degrees of glomerular scarring could be seen. Arterial lesions attributable to hypersensitivity to the antigen were few in number and slight in degree. In the hearts of several animals there were lesions strongly suggestive of Aschoff bodies. Bovine serum γ-globulin disappeared from the circulation much more rapidly than did the albumin; it also excited a much more prompt formation of specific antibody.

Crude bovine serum caused arterial lesions, whose incidence, character, and distribution were essentially similar to those described by Rich and Gregory (*Bull. Johns Hopk. Hosp.*, 1943, **72**, 65). An interesting point observed was the segmental character of lesions in some of the arteries accompanied by large veins, that portion of the arterial wall lying next to the vein being spared. All the arterial lesions in the animals killed at the end of 4 weeks showed reparative changes. Both the albumin and globulin fractions disappeared from the circulation between 2 and 4 weeks after the injection of the crude serum. Precipitins were formed more actively to the globulin than to the albumin component.

The findings are discussed, and the possibility that the changes described may be the products of spontaneous disease in the rabbits is considered in detail and rejected. Reasons [which to the abstracter are not wholly convincing] are given for regarding the lesions as the results of antigen-antibody reactions in the tissues.

G. Payling Wright

2022. **Effect of Phenols on Diphtheria-toxin-toxoid and Antitoxin.** (Über die Wirkung von Phenolen auf das Diphtherie-toxin-toxoid und Antitoxin)

M. EISLER and H. EIBL. *Klinische Medizin* [*Klin. Med., Wien*] **2**, 397–412, May 1, 1947. 11 refs.

This is a preliminary report on the influence of the three dihydroxybenzenes (*ortho* or pyrocatechol, *meta* or resorcin, *para* or hydroquinone) on diphtheria toxins. The authors propose to repeat their investigation with purified toxins which were not at their disposal for the present work. The *in vitro* antigenic properties of different toxins, to which 0·5% phenol had been added, were impaired or abolished after adding 1 ml. of one of the dihydroxybenzenes in dilutions up to 1 in 20 or 1 in 40 to 9 ml. of toxin and incubating the mixture for 24 hours at 37° C. in the water-bath—that is, flocculation was completely or partly prevented when specific antitoxin was added. With non-phenolized toxins only pyrocatechol in a dilution of 1 in 10 proved capable of preventing flocculation. In contrast the action of formol-toxoids as well as of antitoxins was in no way influenced by these substances. The *in vivo* actions of the toxins—production of oedema, haemorrhage and necrosis—were only slightly diminished by pyrocatechol in a dilution of 1 in 10; the influence of the others was minimal. The action of the dihydroxybenzenes is explained by their being fixed as weak acids to basic groups of the toxin. As they display a different action with regard to *in vitro* and *in vivo* tests the authors assume that the properties producing flocculation and erythema-necrosis are caused by different parts of the toxin molecule.

[Thus it would appear that toxins treated with one of the dihydroxybenzenes lose their power to combine with antitoxin while preserving their toxic properties, which is the reverse of the action of formalin.] *R. Salm*

2023. **Reticulo-endothelial Immune Serum (Reis). V. An Experimental Anemia in Bartonella Infected Rats Produced by Anti-blood Immune Serum**

C. M. POMERAT, E. H. FRIEDEN, and E. YEAGER. *Journal of Infectious Diseases* [*J. infect. Dis.*] **80**, 154–163, March–April, 1947. 4 figs., 19 refs.

Paediatrics

2024. **Bone Marrow Infusion in Childhood. Experiences from a Thousand Infusions**
S. HEINILD, T. SØNDERGAARD, and F. TUDVAD. *Journal of Pediatrics* [*J. Pediat.*] **30**, 400–412, April, 1947. 2 figs., 42 refs.

The authors, who work at the University Clinic of Paediatrics, Copenhagen, have had experience of nearly 1,000 bone-marrow infusions in 495 patients. The technique used is that of Køster. The skin is disinfected with iodine, and that part of it over the upper half of the tibia is tightened between two fingers. A special bone-puncture cannula is introduced by a boring motion in the middle of the anterior aspect of the tibia, about 3 cm. below the joint line, and directed a little distally. To make sure that the point is in the marrow space a little marrow is aspirated with a 10-ml. syringe; after the syringe is removed a little blood and marrow should trickle out. No anaesthesia was used in children under the age of 2, but light ether anaesthesia was needed in older patients. The infusion is performed with two 10-ml. syringes, one being filled by an assistant while the other is being used. The maximum rate of infusion is 10 ml. per minute.

After much experience of single, multiple, and continuous infusions of different substances, the authors conclude that single and multiple bone-marrow infusions are quite safe; they have had no complications of any kind. Histological examination of 11 tibiae within 14 days of the infusion revealed no abnormality, nor did *x*-ray examination up to 2 years after infusion. The authors are opposed to continuous infusion because of the risk of osteomyelitis, of which they report 5 cases, and they advise against the infusion of hypertonic solutions on account of the pain. *N. M. Jacoby*

2025. **Feeding of Premature Infants. A Comparison of Human and Cow's Milk**
H. H. GORDON, S. Z. LEVINE, and H. MCNAMARA. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **73**, 442–452, April, 1947. 17 refs.

Carefully controlled clinical studies were undertaken to compare the progress of premature infants given isocaloric amounts of human milk or of mixtures of cow's milk under comparable nursing and medical care, and environmental conditions. The subjects were all healthy prematurely-born infants. Any infant who became ill was excluded from the statistical analysis.

Three feeding mixtures were used: (*a*) human milk, (*b*) evaporated milk, and (*c*) half-skimmed powdered milk. The mixtures were given to the infants in the proportion of 55 calories per pound (0·45 kg.) of body weight. The human milk mixture was low in protein and high in fat and fluid compared with the cow's milk mixtures. The chief difference between the two cow's milk mixtures was the lower fat content of the half-skimmed powder mixture. Both mixtures of cow's milk contained larger amounts of calcium, phosphorus, and other minerals than did the human milk. The mean gain in weight was measured in grammes per kilo per day for a period of 21 days, from the seventh to the twenty-eighth day of life. For the 16 infants fed on human milk the average gain in weight was 12·5 g. per kilo per day, compared with 14·1 g. for the 39 infants fed on evaporated milk and 15·7 g. for the infants fed on half-skimmed milk. The differences were all significant.

The results of this statistical study support the laboratory investigations which suggest that mixtures of cow's milk are more suited for the peculiar needs of premature infants than human milk. This may be due to the higher protein content of cow's milk, although the possibility exists that the higher mineral content of cow's milk is also a factor. Since there is no significant difference in the weight gains for the larger infants (1,621 to 1,996 g.) on the three diets, it seems wise to feed the infants of this weight group on human milk whenever obtainable from individual mothers, in order to stimulate the mother's milk supply and thus permit more infants to be discharged from hospital on breast-feeding.

It is concluded that under conditions of modern hospital practice, mixtures of cow's milk in amounts designed to give approximately 120 calories per kilo will produce larger gains in weight in premature infants than human milk. Mixtures of partially skimmed cow's milk are particularly indicated for smaller premature infants. *Jas. M. Smellie*

2026. **Blood Levels and Absorption of Vitamin A in Children with Keratosis Follicularis**
R. F. KRAUSE and H. B. PIERCE. *Journal of Nutrition* [*J. Nutrit.*] **33**, 633–640, June 10, 1947. 2 figs., 8 refs.

In a survey of 394 children no significant difference was found between the serum vitamin A levels of children with and without folliculosis. The serum carotene values were lower in children with folliculosis. The children of both groups are equally capable of absorbing vitamin A, as indicated by their serum levels after the administration of 50,000 and 25,000 i.u. of vitamin A.—[Authors' summary.]

2027. **Cardio-esophageal Relaxation as a Cause of Vomiting in Infants**
E. B. D. NEUHAUSER and W. BERENBERG. *Radiology* [*Radiology*] **48**, 480–483, May, 1947. 5 figs., 4 refs.

Persistent or recurring vomiting in the newborn or in young infants is a frequent problem. When severe, and especially when persistent regurgitation is alleviated by an erect posture, radiological examination is indicated. By this method during 3 years, the authors have found

12 patients whose symptoms were evidently due to "chalasia" of the cardia or failure of the oesophageal hiatus to contract. Retrograde barium filling of the oesophagus during inspiration or with increase in intra-abdominal pressure with persistent relaxation of the sphincter is diagnostic. The condition appears to be a temporary aberration of the neuromuscular function of the hiatal portion of the oesophagus and of the diaphragm. There were no deaths in the series, and in only one instance had the condition continued beyond the neonatal period. Most cases are relieved if the infant is fed in the erect posture and maintained in this position for 30 minutes. In more severe cases the patient should be kept in a semi-sitting position day and night. Thickening of feeds with cereal may encourage gastric retention.

T. Semple

2028. **Serum Levels of Vitamin A in Children. A Comparison Following the Oral and Intramuscular Administration of Vitamin A in Oily and in Aqueous Mediums** B. KRAMER, A. E. SOBEL, and S. P. GOTTFRIED. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **73**, 543–553, May, 1947. 2 figs., 10 refs.

Histological evidence of avitaminosis-A has been found in children with chronic diarrhoeal disease whose vitamin-A intake was large. Intramuscular injection of an oily solution of the vitamin did not produce a rise in the level of vitamin A in the serum, but an aqueous dispersion did. It was, however, locally irritant. Equally good results were obtained with oral administration of "vifort", an aqueous suspension of fish-liver oil (6,000 units vitamin A in 0·6 ml.) and other vitamins with 11 volumes per cent. of a sorbitan monolaureate polyoxyalkylene derivative as dispersing agent. In normal children the rise in serum level is greater and occurs earlier with the aqueous suspension than with ordinary fish-liver oil. Much greater rises occurred with a suspension containing the same amounts of fish-liver oil as in "vifort" but no other vitamins and 20% dispersing agent. The dispersing agent itself produced no rise. These observations suggest that impaired absorption of vitamin A may be due to failure of emulsification in the intestine.

P. R. Evans

2029. **Dwarfism in Healthy Children: Its possible Relation to Emotional, Nutritional and Endocrine Disturbances** N. B. TALBOT, E. H. SOBEL, B. S. BURKE, E. LINDEMANN, and S. B. KAUFMAN. *New England Journal of Medicine* [*New Engl. J. Med.*] **236**, 783–793, May 22, 1947. 13 figs., 48 refs.

The results are given of a carefully planned and detailed investigation of 51 abnormally short children, from 2 to 15 years of age, attending the paediatric service of Massachusetts General Hospital in the past few years. In the series there were 28 boys and 23 girls; in none was there "definite disturbance in the pulmonary, cardio-vascular, gastro-intestinal, renal, hepatic, skeletal, or endocrinologic system". The study includes the apparent causes of the stunted growth and the results of different types of treatment. The degree of dwarfing is charted for each case; all were "5 cm., or more, shorter than 90% of normal children of the same sex and age". Data of height, weight, calorie intake, social and psychological circumstances, and so forth are compared with those for other groups of children with known pituitary and thyroid disturbance.

In the majority of cases no evidence could be found of a hereditary factor, but the nutritional history showed that many patients presented difficult feeding problems, and had done so from infancy. Of the group a third were underweight, and the majority had a poor fatty covering. The investigation included the study of total calorie, protein, and calcium intakes, and a consideration of their effects upon weight, height, and skeletal maturation. It was concluded that for the underweight children total calorie intake was more important than protein intake.

Attempts to increase the food in the underfed children were in many cases defeated by the refusal of the children to eat more. A high incidence of social and psychiatric difficulties was found in these thin and undersized children. In a few cases mental deficiency seemed to explain the poor intake of food. In others good results were obtained by psychiatric treatment, not only in improved appetite and increased food intake, but also later in increased bony growth and maturation. The authors give a prognosis of "fair to good" from psychotherapy in about half of these psychiatric cases.

The investigation concludes with a discussion and a clinical study of the influence of the pituitary growth hormone in retarding bony growth in this group of "healthy dwarfs". If the growth hormone is sufficient, and the calorie intake insufficient, average growth may continue, but at the expense of body fat. As the children in this series had a daily protein intake of 2 g. per kilo body weight the stunted growth may have been due to "relative deficiency" of the pituitary hormone. This possibility was tested by giving, not the actual pituitary substance, but its substitute, methyl testosterone, to 4 of the thin dwarfs and to 4 well-nourished dwarfs as controls. After 3 months' administration of 20 to 30 mg. daily by mouth there was an increase of growth to "normal and superior levels" in all (both thin and well-nourished dwarfs).

Fuller details of the previous personal and nutritional record of a well-nourished dwarf of 13 years are given. His health had been normal up to 4 years; it had then deteriorated, owing to poverty and neglect, up to 8 years, when he was both thin and short; he was then well cared for, and gained much weight, but did not make good his deficiency in height. In this case no dietetic treatment was given, but he received three courses of methyl testosterone. The first course, successful during its administration, was followed by return to the previous slow growth rate; but after the second course, the increased rate was maintained after the drug was withdrawn, and was unaffected by the third course of testosterone. The results in this case suggest to the authors that the condition had been one of "functional hypopituitarism" produced by privation, and that normal pituitary function had followed the second course of testosterone.

The authors do not recommend testosterone as the initial treatment for dwarfs who are physically sound. The first essential is to correct dietetic errors, either by simple adjustment of the diet or by adjustment of emotional disturbances by psychotherapy. But if this fails methyl testosterone may be tried, especially in adolescent boys. It should be given for one or two short periods only, because " it cannot yet be said that such hormonal therapy is free from permanently harmful effects upon testicular function ". *C. McNeil*

2030. **Further Observations in Dental Defects in Infants Subsequent to Maternal Rubella During Pregnancy**
M. W. EVANS. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 780–785, June 28, 1947. 11 refs.

The coincidence of maternal rubella contracted during pregnancy with dental defects in the children is analysed in 67 cases, 34 of which had been recorded previously by the author. Earlier conclusions are supported by the new evidence.

The time of tooth eruption and the incidence and degree of dental caries and of enamel hypoplasia are the main subjects of the study. The defects are graded according to their severity. Their character chiefly depends on the time of maternal infection. The foetal tissue of tooth structure is most vulnerable to any adverse influence during the first 3 months of pregnancy. Within this period three groups are distinguished: group A, up to the sixth week of pregnancy; group B, from the sixth to the eighth week; group C, from the eighth to the twelfth week. Retardation of eruption of the deciduous teeth—the most striking dental aberration—and enamel hypoplasia prevailed in the " early pregnancy " groups, when the mother was infected before the third month, 1 child in every 2 showing delay of eruption as against 5% of the children of the " later pregnancy " group. Enamel hypoplasia affecting on the average three deciduous teeth was present in approximately 20% of all cases (0·4% is regarded as normal). Congenital absence of deciduous teeth and premature eruption of permanent teeth were also observed in the early groups. The greatest incidence of caries was observed in group B. After the third month of pregnancy infections influence the tooth development insignificantly. In all but 5 cases the dental defects were linked with at least one other congenital malformation due to maternal rubella infection.
M. Dynski-Klein

2031. **Rickettsial Diseases of Childhood. A Clinical Pathologic Study of Tick Typhus, " Rocky Mountain Spotted Fever ", and Murine Typhus, " Endemic Typhus "**
J. C. PETERSON, J. C. OVERALL, and J. L. SHAPIRO. *Journal of Pediatrics* [*J. Pediat.*] **30**, 495–528, May, 1947. 17 figs., 60 refs.

The authors describe 26 cases of Rocky Mountain spotted fever with 7 necropsies and 15 cases of murine typhus in children. The geographical incidence of so-called Rocky Mountain spotted fever extends far away from the Rocky Mountains; the infection should be called simply " tick typhus ". Tick typhus is said to be common in the whole of the United States and to some extent in Central and South America. The incidence of murine typhus is unknown, but it is probably relatively common in the U.S.A.

The chief pathological lesion in tick typhus is an acute arteritis. The arterial lesions are more obvious in the skin and testis than in any other organ. Of more importance, however, is a generalized capillary damage, involving especially the lungs and heart, and causing myocarditis and acute interstitial pneumonia. After an incubation period of 2 to 13 days the onset is abrupt, with severe headache and a macular rash. The patient becomes drowsy and may pass into coma. The authors' patients had slight to moderate generalized oedema. In all but the mildest cases the rash becomes purpuric. There is marked tachycardia and a continuous high temperature. There is a relative leucopenia in the early stages, with a constant reduction in the plasma proteins. Laboratory diagnosis is by the agglutination of *Proteus* OX19 and by complement fixation. Treatment consisted of administration of antiserum in a few cases and *para*-aminobenzoic acid in others. Results of both treatments were promising, but the number of cases treated was too small for a definite conclusion to be drawn.

The pathology of murine typhus is said to be unknown. The onset is with headache and general febrile symptoms. The fever is continuous. The rash appears on the third to the seventh day, first on the trunk as pink macules which may become petechial. There is less constant hypoproteinaemia than in tick typhus and no evidence of cardiac embarrassment. The diagnosis is established by agglutination of *Proteus* OX19. The treatment given was the same as that for tick typhus, but the disease is a much milder one and all the patients recovered.
R. S. Illingworth

2032. **Treatment of Whooping-cough by Intramuscular Injection of Blood.** (Behandling av kikhosta med intramuskulära blodinjektioner)
K. L. MÖLLER. *Nordisk Medicin* [*Nord. Med.*] **34**, 1445–1447, June 27, 1947. 5 refs.

Attempts to immunize children actively against pertussis by administration of a whooping-cough vaccine have been made with some success in the U.S.A. When the child already has whooping-cough, passive immunity must be aimed at. By giving adults who have already had whooping-cough large doses of pertussis vaccine over a long period, so-called hyperimmune human serum has been produced. Various authors have claimed good results with injections of hyperimmune serum and also with γ-globulin. Söderling, in 1943, published his results with intramuscular injections of whole blood (20 to 80 ml.) taken from adults who had had whooping-cough; his results comparing quite favourably with those obtained in America with hyperimmune serum.

Since Söderling's publication intramuscular whole-blood injections have been used for the treatment of severe cases of pertussis in the out-patient department of the Borås Centrallasarett. The blood was usually taken from parents, who had either had pertussis or had

shown themselves to be immune by not developing it after exposure to infection. The blood was citrated. Small children were given 20 ml., older ones 40 ml. by intramuscular injection, half the quantity being given into each buttock. In most cases a second injection was given 2 or 3 days later, and very occasionally a third or fourth.

Most of the 89 children treated were under 4 years of age, and on an average they had been coughing for 19 days and whooping for 10 days before treatment was started. Only severe cases were treated. The result was classified as " good " if the attacks ceased or became much less frequent in 24 to 48 hours after the first injection. In " moderately good " results the frequency or severity of the attacks was noticeably diminished within 24 to 48 hours, though the improvement was not as striking as in the first group. Finally there was a group in which neither frequency nor intensity of attacks was in any way affected, but the improvement in general health was striking; this alone might be considered an indication for the treatment. No complications were seen.

On this basis, 56·2% were classified as " good results ", 20·2% as " moderate ", and 23·6% as without improvement. These results must be attributed to a passive immunity being conferred on the child. That the treatment is really specific is shown by the fact that in some cases the result of the first injection was striking, but transient; hence it was decided to give two injections at intervals of 2 to 3 days. It is probable that the blood of some donors contains fewer antibodies than that of others; this may account for the cases which failed to respond. The results obtained by this simple and cheap method compare favourably with those obtained in the U.S.A. with much more complicated techniques.

Mary J. Wilmers

2033. **Cutaneous Tests and Immunization in Diphtheria and Scarlet Fever**

J. A. Toomey and R. A. Keller. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **73**, 531–542, May, 1947. 15 refs.

Since 1925 Schick and Dick tests have been carried out on student nurses in Cleveland hospitals; 49·7% were Schick-positive. There was no significant difference in this respect between nurses from Cleveland hospitals and those from hospitals in smaller communities, or between those who had had diphtheria and those who had not. Schick-positive nurses were immunized. From the point of view of efficiency, convenience, and reactions after injection, alum-precipitated toxin (0·1 ml. subcutaneously followed by 0·4 ml. the next week, and 1 ml. the next month) is preferred to toxin-antitoxin and to toxoid. In 20 years 0·06% of the nurses have developed diphtheria.

There were 38·9% of Dick-positive nurses. [There are numerical errors in the further analysis of the results (tables 7 and 8).] Nurses were given five immunizing doses of Dick toxin at weekly intervals (500, 2,000, 8,000, 25,000, and 100,000 cutaneous test doses); 28·7% had reactions, usually after the first dose of toxin and usually slight but sometimes causing confinement to bed for 1 to 5 days. Nausea and vomiting and pains in the joints were the most common systemic reactions. Only 1·4% of the nurses have developed scarlet fever after immunization, despite heavy exposure. *P. R. Evans*

2034. **Disease of the Middle Ear in Dysentery in Infants.** (Заболевания среднего уха при дизентерии у детей раннего возраста)

I. D. Bereznyak and V. I. Apostol. Врачебное Дело [*Vrach. Delo*] **26**, 713–718, 1946.

The authors have investigated the frequency of otitis media in infants suffering from dysentery and the effect of this complication upon the course of the disease. In all 96 infants were studied, 53 male and 43 female, aged up to 2 years. All were undernourished, and rickets was common; 40 had a mild or moderate attack of dysentery, and the remainder a severe one. The incidence of otitis media was 14·8%. The mortality was 4·9%, and 14% in those cases where mastoiditis occurred as well. The infection was bilateral in 73% of cases. The diagnosis of otitis media during the course of dysentery is difficult. Changes in the tympanic membrane are not marked and are not a reliable guide to the severity of the process; attention is usually drawn to the presence of the complication by a worsening of the general condition not attributable to the alimentary infection. *D. J. Bauer*

2035. **Alexander's Rabbit Serum in the Treatment of Influenzal Meningitis. An Evaluation of its Use in Conjunction with Sulfonamide Compounds**

K. H. Beck and F. R. Janney. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **73**, 317–325, March, 1947. 3 figs., 2 refs.

Cases of influenzal meningitis were treated with sulphonamides and Alexander's anti-influenzal rabbit serum. Of 47 patients studied 27 recovered, in 5 of whom there were sequelae. Early diagnosis is important. Sulphonamides must be given in high concentration, and anti-influenzal serum should be preceded by intravenous fluid therapy. Better results were obtained with a combination of sulphonamides and serum than with the former alone.

[This paper was written before treatment with streptomycin was introduced.] *A. G. Watkins*

2036. **Celiac Syndrome. VI. The Relationship of Celiac Disease, Starch Intolerance, and Steatorrhea**

D. H. Andersen. *Journal of Pediatrics* [*J. Pediat.*] **30**, 564–582, May, 1947. 11 figs., 8 refs.

The nature of coeliac disease is discussed, but not such causes of the syndrome as cystic fibrosis of the pancreas, stenosis of the ileum, or chronic enteric infection due to ascaris, giardia, or salmonella. The author defines coeliac disease as chronic or recurrent diarrhoea occurring between the sixth month and sixth year, without demonstrable bacteriological or anatomical basis, in which the child is intolerant of a normal diet for the age, responds to dietary therapy, and at some time has a protuberant

abdomen, and gains slowly in weight. She does not consider the presence of steatorrhoea necessary for the diagnosis. She discusses the findings in 83 cases which satisfy the above criteria.

In one-third of the cases indigestion, usually with diarrhoea, began before the age of 6 months, in another third between the ages of 6 and 12 months, and in the remaining third between 1 year and 3 years. In the majority of cases episodes of diarrhoea began with an upper respiratory infection, and were controlled by dietary restriction or by administration of sulphadiazine. The author states that such episodes are often followed by a "critical period" in which the classical signs of coeliac disease appear. These are ascribed to a multiple deficiency state grafted on to the basic constitutional disease. Patients then pass into the "maintenance phase", in which for a year or so after recovery of normal weight there are brief recurrences of diarrhoea precipitated by a respiratory infection or a break in diet.

Steatorrhoea is not considered to be part of the basic process. It is transitory and disappears within 2 months of the start of intensive dietary and vitamin therapy. Some patients who present the complete physical appearance of coeliac disease and who excrete large pale foul stools do not, in fact, have an excess of fat in the faeces. The steatorrhoea may be the result of deficiency of some dietary factor required by the intestine for the normal absorption of fat. Clinical evidence, including the response to treatment, suggests that this substance is part of the vitamin-B complex. The author considers that the most important part of the basic constitutional disease is a deficiency of pancreatic amylase, associated with an excess of starch in the faeces and clinical intolerance of starch. These characteristics persist throughout the course of the disease, and constitute the objective findings that are of most value in diagnosis. In all the author's cases there was a considerable reduction or absence of amylase in the duodenal juice. Three difficulties are encountered in the assay of the amylase: the admixture of gastric juice with the duodenal juice, the presence of saliva as a result of the commonly associated hypochlorhydria, and the normal absence of amylase from the duodenal juice in the neonatal period and the small quantity normally present in the remainder of the first year of life. This last difficulty renders the estimation of amylase concentration useless as a diagnostic test in the first 6 months of life. Protein metabolism is also considered to be disturbed, as shown by the high requirement of dietary protein and a tendency to hypoproteinaemia on a normal diet.

The diet recommended is one of high protein, limited fat, and high carbohydrate. The carbohydrate consists of simple sugars or disaccharides, glucose, banana, and fruit juices in the acute stage, followed by the addition of cooked vegetables, raw apples and pears. Cereal starches, bread, and potatoes are withheld for a year or more after recovery and then only given with great caution. Vitamins are given in the form of vitamin-B complex, vitamin C, and fish-liver oil concentrates, all by mouth, in a quantity equal at least to double the estimated normal adult requirement.

R. S. Illingworth

2037. **Empyema Thoracis in Infants and Children**
A. E. CHAPLIN. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **22**, 91–105, June, 1947. 2 figs., 52 refs.

The author has analysed in a series of tables 275 cases of empyema in children and infants into age groups, with regard to mortality and bacteriological study. Pre-sulphonamide and post-sulphonamide periods, each of 5 years, are compared, and the value of this treatment in the prevention of post-pneumonic empyemata is assessed. The resistance of staphylococcal empyemata to sulphonamides is shown.

The first part of the paper demonstrates the effect of sulphonamides on the incidence, mortality rates, and bacteriology, the two 5-year periods being 1934–8 and 1940–4. The table reveals the reduction in pneumococcal and streptococcal empyemata and in staphylococcal empyemata in children of 2 to 14 years, but emphasizes that there is no effect upon either the incidence or mortality from staphylococcal empyemata in infants under 2 years; in the latter group staphylococcal empyema is slightly more frequent than pneumococcal. The general mortality rate for infants under 2 years for all bacterial types was 64.

The second part of the paper deals with the use of penicillin in the treatment of sulphonamide-resistant pneumonia, and of empyema due to penicillin-sensitive organisms. Penicillin given systemically and intrapleurally, coupled with aspiration of pus and instillation of penicillin into the pleural cavity every 2 to 3 days, may result in complete resolution of empyemata due to penicillin-sensitive organisms in infants under 1 year; success is unlikely after this age. There were good results with only 1 death in a collected series of 21 cases of penicillin-treated empyemata in children and infants. The need for surgical drainage in many cases and the limitations of the aspiration-penicillin replacement method are discussed.

[This excellent paper is difficult to abstract because so much of its worth lies in the comprehensive tables given. Some radiographs are also reproduced.]

R. E. Bonham-Carter

2038. **Early Evidence of Psychoses in Children. With Special Reference to Schizophrenia**
C. BRADLEY. *Journal of Pediatrics* [*J. Pediat.*] **30**, 529–540, May, 1947. 11 refs.

Investigations were made on 138 maladjusted children in a children's psychiatric hospital. In 14 cases the patients were considered potentially schizophrenic and all were under 13 years of age. The children's reactions were noted only by persons entirely unfamiliar with each patient's background and were checked by several members of the staff who had worked with the entire group. Past histories and present states were examined. Schizophrenia was defined for the purpose of this study as a condition, "peculiarly distinguished by a diffuse retraction of interest from environment". It is noted that in childhood particularly there is no generally accepted definition of the psychoses.

In the schizophrenic group seclusiveness, irritability

when disturbed, day-dreaming, bizarre behaviour, diminution of personal interests coupled with the regressive nature of these, sensitivity, and physical inactivity were especially prominent, in that order of frequency. The first two symptoms were noted particularly, even in children of 3 years old. The histories of 39 schizophrenics over a period of 15 years were reviewed, and it was found that maladjustment had been present before the age of 2 in at least 29 cases in the form of lack of interest in persons and surroundings, retarded speech, feeding problems, and hyperactivity. In 6 cases speech developed normally for a time but was lost later in infancy. Mild or brief episodes of schizoid behaviour may develop at times of stress or illness in children who at other times are adequately adjusted, and a definite diagnosis is only justified on repeated observation in a variety of situations. The condition may coexist with mental deficiency, epilepsy, cerebral palsy, and other handicaps. Treatment involves elimination of the factors intensifying the patient's maladjustment, and the prognosis is serious. *Beryl Twyman*

2039. **Hypercalcemia and Idiopathic Hyperplasia of the Parathyroid Glands in an Infant**
E. L. PRATT, B. B. GEREN, and E. B. D. NEUHAUSER. *Journal of Pediatrics* [*J. Pediat.*] **30**, 388–399, April, 1947. 14 figs., 12 refs.

An infant was studied by the authors from the age of 15 weeks until its death at 10 months. The leading symptoms were weakness, hypotonia, lethargy, anorexia, and malnutrition. Investigations revealed a constantly high blood calcium with low urinary calcium excretion and deficient renal function. Radiographs of bones showed some hypocalcification, and a biopsy revealed fibrosis of the marrow spaces.

At necropsy there was very slight enlargement of the parathyroids, which microscopically showed lack of stroma, great cellularity, and increase in chief cells and transitional water-clear cells. Some nephrocalcinosis and a calcium plaque in the aorta were seen, but no other metastatic calcification was observed. The bones showed osteitis fibrosa. The apparently unique association of hypercalcaemia with chief-cell hyperplasia is discussed, but no satisfactory explanation is offered.
N. M. Jacoby

2040. **Thiouracil in Childhood Hyperthyroidism**
L. P. WILLIAMS and F. R. JANNEY. *Journal of Pediatrics* [*J. Pediat.*] **30**, 371–380, April, 1947. 2 figs., 13 refs.

Six female children, between the ages of 7 and 10 years, suffering from mild hyperthyroidism were treated with thiouracil in the Milwaukee Children's Hospital. The basal metabolic rate (B.M.R.) in 5 children was about +25%, and in the sixth +41%. Symptoms were mild in all cases, and although exophthalmos was present in only 2 children all showed definite enlargement of the thyroid. The patients were put to bed and thiouracil was administered in a dosage which varied from time to time " according to present needs and previous response ".

Dosage in each case was as follows: (1) In a child, aged 10, the B.M.R. was +26%; thiouracil, 0·2 g., was given daily for 6 weeks (B.M.R. then −9%). The child was allowed up, and the dose reduced to 0·1 g. daily. Five weeks later, because of accidental omission of the drug, the B.M.R. rose to +28%. Thiouracil, 0·4 g., daily was given for 4 weeks (B.M.R. +3%), then 0·2 g. daily for 3 months (B.M.R. −2%), followed by 0·1 g. daily for 4 months (B.M.R. +8%), and finally 0·05 g. daily for 4 months when treatment was stopped. (2) In a child, aged 14, the initial B.M.R. was +25%. The child received thiouracil, 0·1 g., twice daily for 2 weeks (B.M.R. unchanged), then 0·4 g. daily for 2 weeks (B.M.R. +23%), then 0·2 g. daily. During the next 7 months the drug was taken irregularly (B.M.R. rose to +37%). The child was given 0·4 g. daily for 2 weeks (B.M.R. +23%), followed by 0·2 g. for 3 months (B.M.R. +8%), 0·1 g. for 2 weeks, and finally 0·05 g. (3) In a child, aged 10, the initial B.M.R. was +24%, and 0·1 g. thiouracil was given three times a day for 2 weeks (B.M.R. −3%), followed by 0·1 g. daily for 2 weeks (B.M.R. +17%), 0·2 g. daily for 6 weeks (B.M.R. +12%), 0·15 g. daily for 3 months (B.M.R. −7%), and finally 0·5 g. daily for 6 weeks. (4) Treatment continued for 9 months in a child, aged 13, the initial dosage being 0·4 g. daily. (5) The B.M.R. was not at first determined in the fifth child, aged 9. After a dose of 0·4 g. daily the white cells fell to 4,400 (32% neutrophils) per c.mm. The dose was reduced to 0·2 g. daily for 2 weeks. The B.M.R. was then +22%, white cells 6,500 per c.mm.; the white cell count did not fall again. With a dose of 0·15 g. daily for 1 month and then 0·1 g. daily thyrotoxic symptoms recurred. Owing to the neutropenic tendencies of the larger dosage the drug was changed to propylthiouracil; observation continues. (6) In a child, aged 7, with an initial B.M.R. of +21%, treatment continued for 9½ months, the initial dosage being 0·3 g. daily.

The authors cannot yet state whether the cure is permanent in these cases, as the period of observation has been too brief; they think that Case 5 may require subtotal thyroidectomy. This patient was apparently the only one who had any toxic symptoms or neutropenia as a result of the treatment. *N. M. Jacoby*

2041. **Dysontogenetic Pituitary Cysts. (Pituitary Cachexia in Childhood)**
H. S. BARR. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **22**, 118–127, June, 1947. 6 figs., 60 refs.

Two cases of pituitary cachexia in childhood were described. Both were due to large colloid cysts of Rathke's cleft with pressure atrophy of the anterior lobe. The designation " dysontogenetic pituitary cysts " for this type, and a classification of the various pituitary cysts are proposed. The reasons are pointed out why the designation " tumours of Rathke's pouch " for craniopharyngiomata is considered to be a misnomer. The pituitary cachexia was associated with syringomyelia in one case and with fibrocystic dystrophy of the pancreas in the other. The possibility of a causal link between the latter and the pituitary disease is discussed.—[Author's summary.]

Medicine: General

2042. **Immersion Hypothermia**
E. WAYBURN. *Archives of Internal Medicine* [*Arch. intern. Med.*] **79**, 77–91, Jan., 1947. 1 fig., 19 refs.

Five airmen were studied after they had been immersed in the North Sea at water temperatures of 58° F. (14·4° C.) or above following long operational flights. A sixth airman had been immersed in water at 43° F. (7·2° C.); this man alone had a subnormal body temperature (93° F.: 34° C.), was in coma, and had auricular fibrillation and flutter, haemoconcentration, and hyperglycaemia. Two other men were semicomatose, one other had auricular fibrillation and flutter, and two had minimal prolongation of auriculo-ventricular conduction time. No other biochemical changes were noted and all patients recovered. The clinical picture depends on the water temperature, the length of exposure, emotional factors, and the specific response to cold of the individual. The treatment recommended is that for shock with rapid restoration of body temperature. Adrenaline administration is contraindicated. A brief summary of a report to Himmler on refrigeration experiments on prisoners in German concentration camps is given.

[The effects of cold were reviewed by Macdonald Critchley, *Med. Annu.*, 1944, **62**, 78.] *W. A. Bourne*

ALLERGY

2043. **Lysis *in vitro* of Sensitized Leucocytes by Ragweed Antigen**
T. L. SQUIER and H. J. LEE. *Journal of Allergy* [*J. Allergy*] **18**, 156–163, May, 1947. 2 figs., 6 refs.

The presence of persistent leucopenia in certain cases of drug hypersensitivity suggests that circulating leucocytes may be destroyed. Lysis of erythrocytes by direct action between red cells and antigen is known to occur, with consequent haemolysis, and it seems probable that there may be a similar reaction sometimes between white cells and antigen.

A series of experiments were made at the Marquette University School of Medicine to determine whether destruction of leucocytes occurred when heparinized blood from ragweed-sensitive subjects was mixed with ragweed-pollen antigen at room temperature. After 1 hour the leucocyte count of such a mixture fell markedly. This fall mainly affected the polymorphonuclear series. The mean fall in twelve experiments was 43%, but when normal saline was added to the blood instead of ragweed antigen the fall was only 10%. When the blood was first heated to 56° C. for 1 hour inactivation of the reagin occurred and there was no comparable fall in the leucocyte count; nor was it apparent in control subjects insensitive to ragweed or in ragweed-sensitive patients who had been successfully desensitized.

R. S. Bruce Pearson

2044. **Antibodies to Ragweed Extract. Demonstration by Collodion Particle Technique in Immune Rabbit Serum but not in Serum of Treated Patients**
O. SWINEFORD and R. HOULIHAN. *Journal of Allergy* [*J. Allergy*] **18**, 190–195, May, 1947. 11 refs.

This paper records the unsuccessful attempt at the Allergy Clinic, University of Virginia Medical School, to measure the thermostable or blocking antibody which Cooke showed to be present in the serum of successfully treated pollen-sensitive subjects.

Suspensions of collodion or "parlodion" particles mixed with pollen extracts under various physical conditions were added to dilutions of sera from control, pollen-sensitive untreated, and previously densitized pollen-sensitive subjects. Agglutination in low titre due to non-specific antibodies occurred in all subjects, but in no case could specific agglutination in high titre be demonstrated. In rabbits immunized by repeated injections of ragweed pollen it was found that non-sensitized collodion particles failed to adsorb specific agglutinating factors, though non-specific antibodies were adsorbed. Agglutination in high titre occurred when collodion particles sensitized with pollen extract were added to the serum. No such agglutination occurred in rabbits who had not been previously immunized. The different effects of human and rabbit sera on ragweed-sensitized particles have not been explained.

R. S. Bruce Pearson

2045. **Pollen Tolerance. Its Bearing on the Treatment of Hay Fever.**
F. M. RACKEMANN. *Journal of Allergy* [*J. Allergy*] **18**, 164–175, May, 1947. 6 figs., 10 refs.

Since the original work of Noon on the desensitization of pollen-sensitive patients, it has been recognized that the degree of tolerance which can be induced in different subjects varies widely. The author observes that during treatment general reactions tend to occur at a definite level of dosage, and he refers to this as the "level of absolute tolerance". This level appears to be more or less constant for one patient in any one season, and it is unwise and unnecessary to attempt to increase the dose of pollen above it. In the next season the initial injection can be given with reasonable safety at slightly below this level, provided a pollen extract of uniform potency is used, and the dose can then be increased to the "level of absolute tolerance" with a few injections only. In this way good results can be obtained with a smaller number of injections than usual, sometimes with as few as four or five per season. The author points out, however, that the level of tolerance can only be discovered by trial and error, and that it bears no constant relation to skin tests or to the severity of symptoms in any particular patient. Furthermore, it does not always

remain constant for a patient from season to season, and not uncommonly decreases, so that a systemic reaction occurs with an extract safely tolerated in previous years. General reactions are treated by injections of adrenaline. Careful case records must be kept if this method of treatment is to be used.

[If this work is confirmed, it will be important for those attempting to desensitize patients to realize that there is no object in trying to increase the dosage of pollen beyond that at which a general reaction has occurred, and that good clinical results can be obtained by keeping the dose slightly below this level. The method of beginning injections at a relatively high level of dosage in patients with a high level of tolerance entails considerable risk in inexperienced hands, however, because the level of tolerance may have fallen since the previous season; in such a case a severe general reaction is more likely than it would be if the dosage were increased steadily from a low level. In Britain adrenaline is usually given in the same syringe with each desensitizing injection, and this is believed to reduce the likelihood of a general reaction, to diminish its severity if it occurs, and to permit the maximum dose of pollen to be attained more quickly.] *R. S. Bruce Pearson*

2046. **The Antihistamine Action of N-(2-Pyridyl)-N-(2-Thenyl)-N′, N′,-Dimethylethylenediamine Hydrochloride**
H. M. Lee, W. G. Dinwiddie, and K. K. Chen. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **90**, 83–87, May, 1947. 2 figs., 18 refs.

This substance, serial number 01013, differs from "pyribenzamine" in having a thiophene in place of a benzene ring. It has been shown to antagonize histamine action on isolated guinea-pig ileum, on the intact animal placed in an atmosphere containing histamine, and on the blood pressure of the anaesthetized cat. It has little or no action of the atropine type, in that it caused no dilation of the pupil when instilled into the rabbit's eye, and no reduction of submaxillary secretion caused by pilocarpine given to the dog. It appears to be a specific histamine antagonist, because, alone, it caused contraction of the isolated rabbit uterus in a strength of 1 in 20,000 to 1 in 50,000. It potentiates the effect of adrenaline on blood pressure. It appears to be relatively non-toxic, the LD 50 for mice on intravenous injection being about 20 mg. per kilo, rather more than that of pyribenzamine but less than that of "benadryl". Given by mouth (25 mg. once or twice a day) it has relieved symptoms in a few cases of hay-fever.

Reginald St.A. Heathcote

2047. **The Treatment of Serum Sickness with Benadryl**
J. C. Peterson and L. K. Bishop. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **133**, 1277–1280, April 26, 1947. 3 figs., 7 refs.

"Benadryl" was completely effective in controlling symptoms in 9 out of 10 cases of serum sickness in infants and young children. In 3 cases the reaction followed the use of highly refined type B anti-*Haemophilus-influenzae* rabbit serum. In the tenth patient the improvement was not complete. The action is only suppressive, since relapse occurs if benadryl is discontinued during the time the illness might be expected to last. A dose of 100 mg. orally abolished symptoms within 2 to 3 hours. It is recommended that a dose of 50 to 100 mg. be given every 6 to 8 hours. It is noted that procaine, benadryl, "pyribenzamine", and ethylenediamine (in aminophylline), all contain in their molecule an aminoethyl group and are effective in serum sickness.

Derek R. Wood

2048. **Effect of Antihistamine Drugs on Increased Capillary Permeability following Intradermal Injections of Histamine, Horse Serum and Other Agents in Rabbits**
M. R. Last and E. R. Loew. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **89**, 81–91, Jan., 1947. 38 refs.

This paper describes work done to determine whether the new antihistamine drugs, "benadryl" and "neoantergan", can prevent the increase in capillary permeability caused by intradermal injection of histamine; and, if so, whether they can act in a similar manner and thus antagonize drugs, parts of whose action is alleged to be due to the setting free of histamine in the tissues. The trypan-blue test was used as the criterion of increased capillary permeability. It was applied to adult albino rabbits, which were used in pairs, one of each pair being given the drug under test and the other serving as control.

Both drugs in a dosage of 5 mg. per kilo body weight almost completely blocked the action of histamine in concentrations of 0·1 mg. per ml. or less. There was a significant difference in the frequencies of the response to concentrations of 0·5 mg. per kilo of histamine in animals given 5 mg. per kilo of neoantergan or 10 mg. per kilo of benadryl. With both drugs a qualitative reduction in the severity of the response to concentrations of 1 mg. per ml. of histamine was observed, but no significant difference in the frequency was found.

Trypsin, snake venom, and staphylococcus toxin were studied, since it has been shown that they give positive trypan-blue responses and can give rise to release of histamine in fixed tissues. No evidence of any protection by the antihistamine drugs was obtained. Similarly, neither affected the trypan-blue response to "tetracaine" or to codeine. Mecholyl was given to animals to see whether the prolonged vasodilation would cause increase in capillary permeability; this did not happen even with 10 mg. per ml. given intradermally. Rabbits were sensitized with horse serum and the trypan-blue response to the serum was elicited. Benadryl, even in a dosage of 10 mg. per kilo, failed to effect any significant change, qualitative or quantitative, in the response to serum in dilutions of 1 in 1,000 or less. At 1 in 5,000 there was a reduction in the number of positive responses, but this was not significant.

From these experiments it is deduced that the drugs can nullify the action of histamine on capillary permeability. Further, as they do not modify the responses to trypsin, snake venom, and so forth, it is argued that histamine is not the principal agent in causing the reactions to these substances. Again, although histamine is

responsible for many of the symptoms of anaphylaxis, it does not seem solely responsible for increased capillary permeability as found in this condition.

Reginald St.A. Heathcote

METABOLIC DISORDERS

2049. **The Cutaneous Form of Porphyria.** (Konží forma porfyrie)
V. KVASNIČKOVÁ. *Časopis Lékarů Českých.* [*Čas. Lék. čes.*] **86**, 358–360, March 28, 1947. 4 refs.

After a general discussion of clinical aspects of porphyrin metabolism a case of "idiopathic cutaneous porphyria" in a woman of 37 is described. The patient's sister used to develop blisters on the fingers in summer, and the patient suffered for years from the same condition. In the seventh month of pregnancy, blisters, at first clear but later haemorrhagic, appeared on the face and upper limbs with paronychiae on the fingers and photophobia. The condition improved after the confinement. When the patient was seen later the skin was strongly pigmented in the exposed areas and there were a few scattered pustules. Abnormal findings were a high erythrocyte sedimentation rate (110,125), a basal metabolic rate of +20%, high alkaline phosphatase (58 units), high plasma iron (112 γ per 100 ml.) and porphyrin tests in serum and urine "strongly positive". The isomer was not determined, but because of the photosensitivity, the presence of uroporphyrin I was suspected. There was some improvement after treatment with vitamin B_2 and D.

The author mentions the beneficial effect of riboflavine and yeast preparations (Vanotti, *Porphyrine und Porphyrinkrankheiten*, Berlin, 1937). She also refers to the abnormal porphyrin metabolism in strongly pigmented cases of thyrotoxicosis which respond poorly to the usual treatment, and thinks that they might be treated as cases of porphyria, as suggested by Vanotti. The latter described a case of thyrotoxicosis in lead poisoning where he considered abnormal porphyrins to play a part in the development of the thyrotoxicosis; treatment with diiodotyrosine was without effect, but after injections of crude liver extract, glucose, and insulin there was rapid general improvement with reduction in the basal metabolic rate.

H. Pollak

2050. **Pantothenic Acid Treatment of Porphyria.** (Über die Panthothensäurebehandlung der Porphyrie)
K. HOESCH. *Deutsche Medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **72**, 252–254, May 16, 1947. 2 figs., 12 refs.

The author finds that the increased excretion of coproporphyrin produced by sulphonamides (sulphapyridine and "tibatin"—the bis-galactoside of 4,4′-diaminodiphenyl sulphone) is reduced by administration of pantothenic acid. Similarly the uroporphyrin excretion produced by trional is abolished when this vitamin is administered. The pantothenic acid was given in doses of 40 mg. daily intramuscularly; 100 mg. intravenously has produced no ill-effects in man. The satisfactory results of treatment of porphyrinuria with liver extract are probably in part attributable to the high pantothenic-acid content of such extracts. There is experimental evidence that porphyrinuria may result from lack of pantothenic acid, and it is claimed that vitamin B_2 is of value in the treatment of the disease. The author has not as yet investigated the action of pantothenic acid in idiopathic porphyrinuria.

O. L. V. de Wesselow

2051. **The Obese Patient. A Statistical Study and Analysis of Symptoms, Diagnosis and Metabolic Abnormalities. Sex Differences—Treatment.**
H. M. RAY. *American Journal of Digestive Diseases* [*Amer. J. digest. Dis.*] **14**, 153–162, May, 1947. 12 figs.

This is a statistical study and an analysis of the symptoms, diagnosis, metabolic abnormalities, and sex differences in 110 out-patients with obesity, in all of whom the obesity was an incidental finding and not a specific complaint.

The symptoms in order of frequency were: fatigue (74%), nervousness (59%), digestive disorders (38%), joint and muscle pains (35%), headaches (30%), and irritability (29%). The clinical diagnoses were: climacteric syndrome (55%), biliary tract disease (92%), hypothyroidism (35%), cardiovascular disease (33%), nutritional deficiency (26%), anxiety states (21%), and endocrinopathia (18%). A control group showed a markedly lower incidence of these conditions.

The group as a whole had abnormal glucose metabolism, more especially the females, and in 60% there was a rapid glucose-tolerance curve. The author suggests that in the course of years the large amount of carbohydrates eaten by the obese conditions the pancreas to rapid and excessive elaboration of insulin, resulting in the rapid utilization of sugar, followed by a state of hypoglycaemia with a resultant increased appetite and craving for food. One result of this is that the readily available carbohydrate is catabolized and protein breakdown deferred. In consequence much of the latter may be lost, causing a nutritional deficiency. Hypercholesterinaemia (levels of over 200 mg. per 100 ml.) was present in 70% of the females and in 52% of the males. The blood count was low (microcytic hypochromic) in 50% of the females. The basal metabolic rate was below −12% in 50% of the cases.

In the discussion on treatment it is emphasized that there is no set routine, and that treatment must be adapted to the clinical findings and personality of the patient. The following measures are indicated: (*a*) Psychotherapy. It is essential to obtain the patient's co-operation from the start and to give him a clear insight into his condition and into the relation of his specific abnormalities to the excess weight. He must realize that there is no drug which will reduce his weight, and must depend on his own efforts to reduce carbohydrate intake. (*b*) Specific therapy of symptoms, which differs in no way from that used in the non-obese. (*c*) Drugs. The use of thyroid for weight reduction is considered to be unsound and harmful. The value of certain cephalotropic drugs is emphasized; these act by reducing the appetite. Amphetamine was used at first,

but later *d*-desoxyephedrine hydrochloride was found to be more satisfactory, since it had the same effect in half the dosage with a minimum of undesirable side-effects. Although this drug had no effect on the blood pressure in cases of essential hypertension, it must be used with caution in cases of hypertensive cardiovascular disease with coronary artery insufficiency or disease, with or without hypertensive retinopathy, nephropathy, or encephalopathy. [The original paper must be referred to for details of the administration of this drug.] No other drugs, endocrine or otherwise, were found to be of any value. (*d*) Diet and exercise. The patients were given a full explanation of their condition, coupled with instructions to weigh themselves daily, to take a normal helping of proteins at only three meals a day, to eschew fats and high-carbohydrate foods, and to adjust the quantity of food taken so as to bring about a loss in weight of about 2 lb. (0·9 kg.) a week. This routine proved simpler and more effective, especially in the more intelligent patients, than a diet sheet. This treatment resulted in an average loss of weight of 11 lb. (4·95 kg.) in 30 days, and of 24 to 28 lb. (10·8 to 12·6 kg.) in 90 days. *Geoffrey Whittall*

2052. **Glycogen Content of Isolated White Blood Cells in Glycogen Storage Disease**
R. WAGNER. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **73**, 559–564, May, 1947. 11 refs.

In one case of the hepatic form of glycogen storage disease the author showed by repeated estimations made by a micromodification of Pflüger's method, that the glycogen content of isolated leucocytes was 2·7 to 7·4 times higher than in normal leucocytes, the maximal concentration being 3·8%. Glycogen was also recovered from the plasma; it is not known whether it is usually present in the plasma in this disease. It is suggested that this procedure may be used as a diagnostic test in suspected cases. *R. E. Bonham-Carter*

2053. **Changes in Personality Appraisal Associated with a Restricted Intake of B Vitamins and Protein**
C. R. HENDERSON, N. C. WHEELER, H. C. JOHNSON, R. C. COGSWELL, G. H. BERRYMAN, A. C. IVY, T. E. FRIEDMANN, and J. B. YOUMANS. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **213**, 488–493, April, 1947. 2 figs., 6 refs.

The development of the Minnesota multiphasic personality inventory (MMPI) permits objective measurement of abnormal personality, and the present paper describes an experiment designed to illustrate the changes in "personality appraisal scores" which occurred in 7 young men on a diet poor in vitamin-B complex.

The men consumed a normal diet for 12 weeks, and during this period various measurements of physical and psychomotor performance were made in order to establish base-line levels. Personality was assessed at the end of this period. After the control period an experimental diet, which contained restricted quantities of vitamin-B complex and of animal protein, was given for 5 weeks. At the end of the 5 weeks 2 of the men received crystalline supplements of vitamin-B complex and of protein; the supplements were given at the end of 15 weeks to a further 3 men, and at the end of 18 weeks to the remaining 2. During the thirty-sixth to thirty-ninth experimental weeks, all the subjects consumed a luxury diet with crystalline nutrients and 10 g. of yeast daily. During the experimental week "personality appraisal" was made on four occasions and numerous other physical, psychomotor, clinical, and biochemical measurements were made at frequent intervals.

Changes in personality, in physical and psychomotor performance, resting pulse rate, and diastolic pressure occurred only in the associated categories of depression, hysteria, and hypochondriasis. No changes were observed in control subjects or in those with other psychological abnormalities. The changes disappeared, and the subjects returned to normal following the addition to their experimental diet of vitamin-B complex, and also in the final period during which a luxury diet was given. *Geoffrey McComas*

2054. **Lesions Following the Use of Ertron in Rheumatoid Arthritis**
M. BEVANS and H. K. TAYLOR. *American Journal of Pathology* [*Amer. J. Path.*] **23**, 367–387, May, 1947. 16 figs., 12 refs.

Prolonged use of "ertron" (an electrically activated ergosterol) by a 63-year-old woman with rheumatoid arthritis led to hypercalcaemia and extensive calcification in the periarticular and subcutaneous tissues, lungs, heart, and kidneys. Lungs, pancreas, kidneys, and lymph nodes contained also granulomatous lesions with foreign-body giant cells; the authors regard these as additional manifestations of the same disturbance. They give references to other similar reports of calcification of tissues resulting from vitamin-D overdosage. *R. A. Willis*

DIABETES MELLITUS

2055. **The Renal Factor in Alloxan Diabetes**
G. L. DUFF, D. C. WILSON, and G. C. MCMILLAN. *Nature* [*Nature, Lond.*] **159**, 575–576, April 26, 1947. 1 ref.

Jimenez Diaz *et al.* (*Nature*, 1946, **158**, 589) reported that dogs, in which the renal vessels were clamped before and for 10 minutes after the intravenous injection of alloxan (100 mg. per kilo) failed to develop the hyperglycaemia of control animals in which clamping was omitted. The observations recorded in the present paper show, however, that by intravenous injection of alloxan, 200 mg. per kilo in a 5% solution, it is possible to produce diabetes mellitus and necrosis of the islets of Langerhans in rabbits subjected to the same arrest of the renal circulation. The necrosis of the beta cells of the islet tissue was identical with that seen both in control animals given alloxan alone and in 2 rabbits receiving the same dose of alloxan immediately after bilateral nephrectomy.

[Comparable results are reported by Gold (*Nature*,

1946, **157**, 574) who gave alloxan in doses of 175, 150, 140, and 100 mg. per kilo to rats. During the dissection of the renal pedicle in some rats a temporary blanching of the pancreas was observed, which was thought to be due to reflex vasoconstriction. Gold suggests that a similar mechanism in the dog might protect the islets from the toxic action of alloxan during the period of its inactivation.] *H. Whittaker*

2056. **Plasma Proteins. I. Alteration in Diabetic Retinitis**
R. W. SCHNEIDER, L. A. LEWIS, and E. P. MCCULLAGH. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **212**, 462–465, Oct., 1946. 6 refs.

The changes in plasma protein, which are often found in association with uncontrolled diabetes mellitus, were investigated in relation to diabetic retinitis. Of 31 patients with diabetic retinitis 28 showed a fall in albumin and 29 an increase in β-globulin. The restoration of normal values by increasing the protein intake and by adequate control of the diabetes was much more difficult in the presence of retinitis, and impossible if serious renal disease was associated with it. In 4 patients the plasma protein levels returned to normal, and these subjects showed the greatest retinal improvement, suggesting that high protein intake may be useful in addition to the other measures employed for the relief of diabetic retinitis. *E. F. Scowen*

2057. **The Fallacy of the Exton-Rose Glucose Tolerance Test**
P. H. LANGNER, M. J. ROMANSKY, and E. D. ROBIN. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **212**, 466–470, Oct., 1946. 22 refs.

The physiological basis of the Exton-Rose glucose tolerance test is discussed, and it is concluded that the basis is unsound since: (1) it depends on a peak figure of the blood sugar for its interpretation and not on the blood-sugar values up to 3 hours after ingestion of glucose; the time relation of the peak varies considerably without necessarily being significant; (2) the paradoxical law of Allen is not applicable to the short periods of time, such as 30 minutes, used in this test.

A comparison of results in the same individuals from the Exton-Rose test and the standard single-dose test is reported, together with the relevant data from the literature. After the administration of 100 g. of glucose in one dose, or in two doses of 50 g. at half-hour intervals, the blood-sugar curve is essentially the same.
E. F. Scowen

2058. **Glycosuria in Recruits. Incidence and Classification**
J. A. KEEPING and R. D. LAWRENCE. *Lancet* [*Lancet*] **1**, 901–903, June 28, 1947. 9 refs.

Between 1939 and 1944, 956 recruits in whom glycosuria had been found at medical boards were subjected to further investigation. In all cases urine tests and blood-sugar estimations were made, and all but 58 were submitted to a full sugar-tolerance test. Of the 956 cases so referred, glycosuria was confirmed in 782. The classification is based on three concepts: (1) The normal blood-sugar curve has a fasting level below 120 mg. per 100 ml., does not rise above 180 mg. per 100 ml. after the ingestion of glucose, and returns to a normal fasting level within 2 hours. During this time there is no sugar in the urine. (2) The normal renal threshold for sugar is 180 mg. per 100 ml. (3) After the ingestion of glucose the blood-sugar level in venous blood is 10 to 50 mg. per 100 ml. lower than in capillary blood as a result of absorption by the tissues. All figures used in the classification are for capillary blood; where venous blood has been used the critical limits have been reduced by 10 mg. per 100 ml.

In 18% of patients diabetes mellitus was demonstrated; 65% had renal glycosuria, and 13·8% oxyhyperglycaemia with a lag-storage curve. The remainder were listed as unclassified with either minor or major variants.
Geoffrey McComas

2059. **The Physical Examination of the Pancreas in Diabetes.** (Znaczenie fizycznego badabia trzustki w wykrywaniu jej chorob u cierpiacych na cukryce)
J. W. GROTT. *Polski Tygodnik Lekarski* [*Polsk. Tyg. lek.*] **2**, 451–454, April, 1947. 1 fig., 16 refs.

According to the author the physical examination of the pancreas in diabetics has been generally neglected. He describes his own technique of examination, which involves palpation of the pancreas, inspection for trophic changes of the skin in the appropriate abdominal region, and a search for hyperaesthesia in the pancreatic zone. Palpation is carried out with the patient lying on his back and his fists supporting the lumbar spine. The examiner overcomes the resistance of the abdominal wall by pressure with his left hand on the left rectus, and palpates the pancreas with his right fingers. In this way enlargement of the pancreatic body and tenderness can be discovered. The atrophic changes affect the subcutaneous fat and there is an increase in the elasticity of the skin over the pancreas. By this method 2,000 diabetics were examined, and in 375 cases (31%) the findings were positive. Among these 375, tenderness on palpation was found in 63% (19% of all examined). Trophic skin changes were present in 59% (18% of the total), hyperaesthesia in 12% (3·6%), and enlargement of the pancreas in 12% (3·6%). The positive findings were especially frequent in recent cases of diabetes (of less than 6 months' duration). The author believes that his findings support the view that chronic pancreatitis often occurs in diabetes.
J. T. Leyberg

2060. **On the Induction of Diabetes by Means of Alloxan**
J. H. GAARENSTROOM. *Journal of Endocrinology* [*J. Endocrinol.*] **5**, 103–110, April, 1947. 13 refs.

2061. **Hepatic Blood Flow and Glucose Output in Normal Unanesthetized Dogs**
A. LIPSCOMB and L. A. CRANDALL. *American Journal of Physiology* [*Amer. J. Physiol.*] **148**, 302–311, Feb., 1947. 35 refs.

Cardiovascular Diseases

2062. **Observations on the Volume of the Pulmonary Circulation and its Importance in the Production of Cyanosis and Polycythemia**

H. B. TAUSSIG and A. BLALOCK. *American Heart Journal* [*Amer. Heart J.*] **33**, 413–419, April, 1947. 3 refs.

In cases of the tetralogy of Fallot the fact that a proportion of the blood short-circuits the lungs results in a diminution of the oxygen content of the arterial blood. If the arterial oxygen saturation is not lower than 65 to 70% the patient may indulge in unrestricted activity, but at levels below this polycythaemia is likely to develop. Should the circulation to the lungs be increased by a successful anastomosis of the innominate artery to one of the pulmonary arteries the arterial oxygen saturation usually rises to 75 or 88%. Following this increase in arterial oxygen saturation, the stimulus to the production of polycythaemia ceases, and over a period of weeks there is a steady decline in the haemoglobin value, red cell count, and haematocrit value in these patients; finally, after several months, these values have returned to normal. Observations on 12 cases are given.

H. E. Holling

2063. **Effect of Elevated Body Temperature on the Cardiovascular System and the Electrocardiogram with Special Emphasis on the Chest Leads**

G. X. SCHWEMLEIN. *Archives of Physical Medicine* [*Arch. phys. Med.*] **28**, 165–174, March, 1947. 3 figs., 38 refs.

This investigation was carried out in patients, aged 19 to 32 years, with venereal disease who were being treated by physically induced fever. The cardiovascular system was normal in each case. Fever was induced by the Kettering hypertherm, and supplementary oxygen was given by means of a nasal catheter at the rate of 4 to 6 litres per minute. In addition to the conventional limb leads, chest leads CF_2, CF_3, CF_4, and CF_5 were recorded immediately before and after fever therapy and in the morning for 3 consecutive post-fever days. No significant electrocardiographic changes were noted in 3 men with acute gonorrhoeal epididymitis and 2 women with acute gonorrhoeal endocervicitis who received physically induced fever at 106° F. for 6 hours. Among 18 patients with secondary or early latent syphilis who received the same fever therapy for 6 to 8 hours and in addition 84·6 to 152·1 mg. of arsenoxide (" mapharsen "), there were 5 in whom changes were recorded in chest leads CF_2, CF_3, and CF_4. These changes consisted of alterations in the amplitude of the T wave of at least 2 mm. Three of these patients showed evidence of dehydration during fever therapy. Of 17 patients who received fever therapy for 3 to 6 hours, combined with doses of sodium penicillin ranging from 600,000 to 1,200,000 units, comparable changes in the chest leads were noted in 3, none of whom showed signs of dehydration during or after treatment. In no case was there any clinical evidence of cardiovascular collapse or coronary insufficiency, and in every instance the electrocardiogram returned to normal within 3 to 14 days. The heart rate increased by an average of 6 beats per minute. The suggestion is made that these electrocardiographic changes are due to reversible myocardial changes resulting from anoxia possibly caused by the increased rate and inadequate filling of the heart. The absence in this series of any changes in the limb leads reported by previous investigators is attributed to the prompt correction of disturbance in the patients' water balance, which was a routine part of the treatment.

[While some of the T-wave alterations recorded are undoubtedly significant there are others which are of doubtful import in view of the notorious lability of the T wave, even in health.] *William A. R. Thomson*

2064. **The Effect of Digitalis on the Fluid Distribution of the Body**

C. A. HANDLEY and J. TELFORD. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **89**, 97–100, Jan., 1947. 8 refs.

Digitalis is known to reduce blood volume in the normal subject and in the patient with heart disease, whether compensated or not. In the case of heart failure the reduction in blood volume can be attributed to the improved cardiac action and lowered venous pressure. In the normal subject some other mechanism must be concerned. The pooling of blood in the liver and spleen has been regarded as the cause. The present work describes attempts to measure simultaneously any changes in the blood volume and the extracellular fluid.

Dogs weighing 10 to 15 kg. were used. The plasma volume was determined with the dye T-1824 and the extracellular fluid with sodium thiocyanate. Less than 15 ml. of blood was required for these estimations and for a haematocrit determination. There were two groups of animals, those under light pentobarbitone anaesthesia and those not anaesthetized. No variation in fluid differences could be observed between the two groups, but the anaesthesia prevented vomiting. The observations show that there is a steady increase in haemoconcentration for several hours. There is a reduction of 20 to 30% in plasma volume, and an increase in the extracellular fluid of about 10 to 20%. These changes reached a maximum in 4 to 8 hours but might persist for 3 or 4 days after a single dose of digitalis.

While a diminution in cardiac output may follow the administration of digitalis, attributed by some to storage of blood in the liver and spleen, the increased haematocrit readings show a definite loss of plasma. The increase in extracellular fluid was unexpected, amounting to as much as 500 to 800 ml. in the individual dog. Only a small

part of this could have come from the vascular system, and the rest must have come from the cells. No explanation for this phenomenon is offered. The U.S.P. XII tincture of digitalis was used, one- to two-thirds of a unit per kilo being given intravenously. "Digalen" (0·6 ml. per kilo) was administered in some cases.

Reginald St.A. Heathcote

2065. **The Influence of Heart Size on the Circulation Time**

M. H. NATHANSON and S. R. ELEK. *American Heart Journal* [*Amer. Heart J.*] **33**, 464–476, April, 1947. 6 figs., 14 refs.

The circulation time was measured in 70 patients with compensated heart disease and enlarged hearts. The test solution used was "macasol" (magnesium sulphate 42 g., calcium gluconate 16 g., sodium chloride 0·9 g., copper sulphate 1 mg., water 100 ml.), though the dosage required to produce the end-point—a warm sensation in the throat—is not stated. The mean circulation time was 13·8 seconds ±25%. In some cases the circulation time was checked by using calcium gluconate alone or fluorescein. The heart size was estimated from the tele-roentgenogram by the use of the formula

$$\frac{\pi}{4} \times \text{longest diameter} \times \text{broadest diameter}.$$

There was a rough correlation between the degree of cardiac enlargement and the circulation time, though patients with mitral stenosis had longer circulation times than those with aortic regurgitation or hypertensive disease. This finding suggests that the figure obtained for the circulation time depends not only on the actual rate at which the blood travels in the veins, but also on the volume of blood in which the test substance is diluted on its way.

When there is considerable residual blood in a dilated heart or in congested lungs, the test substance is greatly diluted and therefore takes longer to reach an effective concentration in the end-organ. The relation between the circulation time and the clinical condition of the patient depends on the relative amounts of blood in heart and lungs. Circulation time may be prolonged in the absence of signs of cardiac failure if a quantity of "residual blood" remains in the heart, but will be associated with signs of cardiac failure if the blood remains in the great veins and lungs. *H. E. Holling*

2066. **Comparative Study of Blood Cultures made from Artery, Vein, and Bone Marrow in Patients with Subacute Bacterial Endocarditis**

M. S. MALLEN, E. L. HUBE, and M. BRENES. *American Heart Journal* [*Amer. Heart J.*] **33**, 692–695, May, 1947. 5 refs.

Cultures were made from the arterial and venous blood, and the bone marrow of a series of 88 patients with subacute bacterial endocarditis. The medium used for the marrow culture was broth (2 drops of marrow per 5 ml. of medium). For blood culture, melted nutrient agar in plates was inoculated with citrated blood, 1 ml. per 10 ml. medium, and at the same time broth cultures were set up with 5 ml. of blood per 100 ml. nutrient broth. No inhibitors were used, and cultures were aerobic. Incubation was continued for up to 1 week, 109 sets of three cultures being made from 88 patients; of these, 24 were positive in one or more of the three cultures. Bone-marrow culture gave a positive result in 21 of 24 cultures, and was also positive in 4 of 5 patients receiving penicillin. Bone-marrow culture was occasionally negative when arterial or venous blood cultures were positive. Venous blood gave positive results in 19 of the 24 patients; arterial blood gave 15 positive results. Bone-marrow culture is, therefore, of use in the diagnosis of bacterial endocarditis. *James W. Brown*

2067. **Cardiac Failure in Penicillin-treated Subacute Bacterial Endocarditis**

M. J. FIESE. *Archives of Internal Medicine* [*Arch. intern. Med.*] **79**, 436–448, April, 1947. 11 refs.

In this paper the possible effect of penicillin in promoting or postponing cardiac failure in subacute bacterial endocarditis is considered, and an attempt is made to determine the factors which predispose to cardiac failure even if the vegetations are sterilized. In a series of 40 untreated cases of subacute bacterial endocarditis which came to necropsy, 25% had congestive failure and 80% myocardial insufficiency of varying degree and chronicity. Of 25 patients treated with penicillin 7 died, 4 of them of cardiac failure; of the 18 who are alive, 3 have had cardiac failure; thus, 30% of the penicillin-treated series had cardiac failure. Statistically, therefore, penicillin appears to postpone the onset and reduce the incidence of cardiac failure, while it is obvious that patients surviving embolism or generalized sepsis may live long enough to suffer myocardial insufficiency. With regard to cardiac efficiency after therapy, analysis of the 25 cases indicates that the important factors are the patient's age, the type of lesion, the general clinical appearance, and the height of the temperature. Thus, the likelihood of a fatal outcome was greatly increased in patients over the age of 50, when the average temperature was high, in patients who clinically appeared very ill, and in acquired mitral and aortic disease as opposed to congenital lesions. It seemed in some cases that absorption of vegetations under penicillin, by further distortion of the valve, actually hastened cardiac failure. The importance of early and adequate treatment is emphasized. This necessitates early diagnosis and determination of the organism's resistance to penicillin so that the dosage required can be estimated. *J. L. Markson*

2068. **Cardiac Arrhythmias Complicating Total Pneumonectomy**

E. MASSIE and A. R. VALLE. *Annals of Internal Medicine* [*Ann. intern. Med.*] **26**, 231–239, Feb., 1947. 8 refs.

One of the chief problems attending the removal of a lung is the effect on the heart and the remaining lung of the abrupt shunting of the entire pulmonary circulation through a vascular bed only half as large as normal. The authors find a high incidence of cardiac arrhythmias after pneumonectomy, which cause increased morbidity

and mortality. Pulmonary vessel ligation and collapse of the lung often produce a profound immediate change in the electrocardiogram, as shown by increased amplitude of the P wave, inversion of T, and axis deviation.

In a series of 120 patients 11 had detectable cardiac arrhythmias; 5 had auricular fibrillation, 4 auricular flutter, 1 frequent auricular premature beats, and 1 frequent ventricular premature beats. Six patients had had the right lung removed and 5 the left. The nature of the symptoms and the type and location of the lung disease had no specific relation to the occurrence of arrhythmias. Age was found to be the most important single factor: all patients who developed arrhythmia were 35 years or older, although 42 of the 120 were under 35 (and 15 of these were children). If patients under 35 are excluded, the incidence of arrhythmia rises to 14·3%. There was no significant sex difference. In this small series no difference was noted in the incidence of cardiac irregularity after the two main techniques of mass hilar ligation and dissection with individual ligation of the hilar structures. All cases developed within a week of operation, 6 being noted on the third post-operative day. Three of the patients died, and an extensive pericarditis was found in the 2 examined post mortem. Unusually rapid mediastinal shift and vagal irritation from a septic bronchial stump were not thought to cause arrythmias. Of the 120 patients, 26 had a cardiac abnormality demonstrable clinically or by the electrocardiograph before operation, but only one of these developed an arrhythmia post-operatively. Apart from the 11 cases with abnormal rhythm, another 6 showed some objective evidence of cardiac embarrassment not present before operation. The electrocardiographic appearances of coronary insufficiency were not found in a single patient during the immediate post-operative period, though 1 man had an attack of cardiac infarction 9 months after operation.

Smith and Wilson (*Amer. Heart J.*, 1944, **27**, 176) found experimentally that an auricle rendered irritable by anoxaemia may be made to fibrillate by vagal stimulation, which shortens the refractory period and lessens conductivity. In the operation of total pneumonectomy at least temporary anoxaemia is bound to occur, and vagal stimulation must surely follow the necessarily extensive intrathoracic manipulation. After pneumonectomy constant observation must be maintained in order to recognize abnormal rhythm early; this may be rendered difficult by loud and stertorous breath sounds. Frequent electrocardiograms after operation are advisable, otherwise the true cause of a patient's deterioration may be missed. There may be reversion to normal rhythm after administration of morphine or other sedatives, but if the ventricular rate remains rapid digitalis or quinidine by mouth, or prompt intravenous digitalization, may be required. *E. G. Sita-Lumsden*

2069. **Coarctation of the Aorta. A Review of 104 Autopsied Cases of the "Adult Type", 2 Years of Age or Older**

G. H. Reifenstein, S. A. Levine, and R. E. Gross. *American Heart Journal* [*Amer. Heart J.*] **33**, 146–168, Feb., 1947. Bibliography.

2070. **Clinical Studies on the Relative Incidence of Congenital Heart Disease.** [In English.]

O. Thordarson. *Acta Medica Scandinavica* [*Acta med. scand.*] **127**, 233–260, April 25, 1947. 61 refs.

The author endeavoured to establish the relative incidence of congenital cardiac defects in a non-selected series of medical cases. Of 31,771 medical out-patients seen between 1934 and 1943 at the Medical Out-Patient Department of the State Hospital of Copenhagen a diagnosis of congenital heart disease was made in 85—that is, in 0·27% of all patients and 1·8% of those suffering from organic cardiovascular disease. Of these 85, 64 were over 15 years of age at the first examination and had never been cyanosed or hampered in their ordinary way of life. Seven belonged to the acyanotic group, 41 to the group of *cyanose tardive*; in 15 an anatomical diagnosis could not be made with certainty. The relevant particulars of 63 cases are given in tabular form. Some details of the murmurs heard in cases of congenital heart disease, the radiographic appearance of the heart, and the electrocardiographic findings are briefly discussed.

[It seems surprising that among the 27 cases of the *cyanose tardive* group listed in the table there should have been 15 cases of interventricular septal defect (Roger's disease) and 12 of patent ductus arteriosus, but no case of interauricular septal defect (this diagnosis does not appear in any of the 53 cases in the table). Of the 14 cases in which the diagnosis of pulmonary stenosis was made not a single patient had ever been cyanosed, although patients of ages 21, 23, 27, and 29 are included; the diagnosis seems to have been made on the grounds of a systolic murmur over the pulmonary area and prominence of the pulmonary arch. In only 2 cases was an anatomical diagnosis available.]

A. Schott

2071. **Clinical Features of Patent Ductus Arteriosus with Special Reference to Cardiac Murmurs**

S. A. Levine and A. E. Geremia. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **213**, 385–394, April, 1947. 7 figs., 10 refs.

The accurate diagnosis of the exact anatomical lesion in congenital cardiac disease has only become of practical importance during the last few years because of the use of specific surgical treatment. The authors analyse 37 cases of patent ductus arteriosus, in which the diagnosis was confirmed at operation. The murmur, having both systolic and diastolic components, varies considerably in loudness from case to case. It is generally loudest in the second, but occasionally in the first or third left interspace. It may be transmitted to the back of the chest. A thrill was present in over half the cases. The pulse pressure decreased from an average of 65·2 mm. before operation to 45·5 mm. after operation. There was no typical electrocardiographic pattern. Right axis deviation does not occur. Rare cases exist in which no murmurs, or at least no diastolic murmurs, are audible; a possible explanation of this is that the pressure in the pulmonary artery is as great as that in the aorta and therefore no flow takes place through the ductus. The

persistence of a basal diastolic murmur after operation was found to be due either to the recanalization of the ductus or to bacterial endocarditis which had also involved the aortic valve. In puzzling or atypical cases cardiac catheterization is necessary to establish an accurate diagnosis. *Geoffrey McComas*

2072. **Studies on the Coronary Circulation. II. The Collateral Circulation of the Normal Human Heart by Coronary Perfusion with Radioactive Erythrocytes and Glass Spheres**

M. PRINZMETAL, B. SIMKIN, H. C. BERGMAN, and H. E. KRUGER. *American Heart Journal* [*Amer. Heart J.*] **33**, 420–442, April, 1947. 12 figs., 30 refs.

Two methods of post-mortem study of the coronary circulation are described. In the first, washed red cells labelled with P^{32} are perfused at a constant pressure of 100 mm. Hg into the left coronary artery, and the number of radioactive red cells is determined either by suitably shielded Geiger counters or by autoradiographs. In the second, glass spherical beads, with diameters ranging from 10 to 400 μ, suspended in a radio-opaque mixture are injected under pressures not exceeding 160 mm. Hg into the left coronary artery, and the diameters of the beads issuing from the right coronary artery, coronary sinus, and right and left ventricular cavities are determined by microscopical measurement. By the latter method the maximum size of anastomotic channels in the dead heart can be determined.

By the first method it was shown that after perfusion of radioactive red cells into a branch of the left coronary artery in normal hearts, labelled red cells were found throughout both right and left ventricles. By the second method it was demonstrated that in the normal human heart beads varying from 70 to 180 μ in diameter can pass from the left to the right coronary artery and from the coronary arteries to the coronary sinus. Hence intra-arterial and arterio-venous anastomoses of those maximum diameters are present. It was also shown that the anastomotic channels between the coronary arteries and the ventricles allow beads of 70 to 220 μ in diameter to pass.

The authors conclude from these results and the work of others that the normal human heart has a fairly extensive collateral circulation with varying kinds of anastomotic channels, which, after an acute coronary occlusion, may be able to supply a limited amount of blood to the ischaemic muscle. *E. B. G. Reeve*

2073. **Incidence of Thrombo-embolic Lesions Accompanying Myocardial Infarction**

H. K. HELLIERSTEIN and J. W. MARTIN. *American Heart Journal* [*Amer. Heart J.*] **33**, 443–452, April, 1947. 1 fig., 43 refs.

The important question of whether the danger of thrombosis and embolism following a myocardial infarction is greater than the danger from heparin and dicoumarol therapy is discussed. The material studied was afforded by a series of 2,000 consecutive necropsies performed between 1935 and 1940, among which were 164 instances of recent and remote infarcts of the myocardium. In 160 of the latter, 73 (45%) cases had a total of 111 " thrombo-embolic lesions ", a term which includes pulmonary thrombosis. In 43 of these 160 cases the thrombo-embolic lesions were a main or contributory cause of death. A control group of 100 necropsies, selected at random except that cases of myocardial disease were excluded and the subjects chosen were from the same age group and had the same sex distribution as the group of patients with myocardial occlusion, showed 15 thrombo-embolic lesions; the difference between these two is statistically significant. From a study of 1,600, not necessarily fatal, American and British cases reported in the literature it seems that 11·5% of cases of coronary thrombosis have clinically detectable thrombo-embolic lesions.

In their own necropsy cases the authors paid particular attention to the occurrence of intracardiac mural thrombi; 95 cases showed no evidence of mural thrombi, yet 37 of these had thrombo-embolic lesions. This finding leads the authors to suppose that thrombo-embolic lesions in myocardial infarction do not necessarily originate from an intramural cardiac clot, but that they may be due, particularly in the leg veins, to local thrombus formation secondary to altered blood coagulability and decreased blood flow. Bearing in mind the dangers of anticoagulant therapy the authors conclude that its use is warranted, but only if proper and careful control is available. *H. E. Holling*

2074. **Studies in Breathing, Pulmonary Ventilation and Subjective Awareness of Shortness of Breath (Dyspnea) in Neurocirculatory Asthenia, Effort Syndrome, Anxiety Neurosis**

M. E. COHEN and P. D. WHITE. *Journal of Clinical Investigation* [*J. clin. Invest.*] **26**, 520–529, May, 1947. 4 figs., 21 refs.

The authors used subjective methods to investigate the problem of symptoms referable to the respiratory system in patients with neurocirculatory asthenia (N.C.A.). The controls were healthy soldiers and those convalescent from infected war wounds. As was to be expected, the majority of the N.C.A. patients had complaints referable to breathing: these were more obvious during the performance of standard exercise tests. The investigators show clearly that the respiratory abnormalities in N.C.A. are not always subjective alone. More interesting conclusions in this paper are: (1) the frequency of symptoms referable to the respiratory system in N.C.A., effort syndrome, and anxiety neurosis is high; (2) at rest, while oxygen is being breathed, the respiratory rate is rapid and the breathing abnormally shallow; (3) while air is breathed the minute respiratory volume is significantly higher in N.C.A. at rest and during moderate exercise than in controls, becoming lower as hard exercise progresses; (4) immediately after exercise N.C.A. patients, as compared with controls, show the greatest disproportion in pulmonary ventilation, suggesting a relation to the high blood lactate and oxygen debt mechanism; (5) vital capacity is normal but the ventilation index is high in N.C.A.; (6) the incidence and severity

of dyspnoea are out of proportion to the severity of exercise, the pulmonary ventilation, or the ventilation index; (7) efficiency of ventilation is low in N.C.A. in both moderate and severe muscular exercise.

A. I. Suchecki

2075. **Evaluation of Vasomotor Tone in Animals and Man by Means of the Tetraethylammonium Ion**
G. K. Moe, B. Rennick, S. W. Hoobler, R. Neligh, and R. H. Lyons. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **32**, 311–312, March, 1947.

Tetraethylammonium compounds, which block autonomic ganglionic transmission, cause in anaesthetized dogs a fall in blood pressure down to a minimal value beyond which further doses cannot depress it. If blood pressure has been raised by carotid clamping or vagal section this response is increased. If it has been raised by adrenaline the response is diminished or absent. If blood pressure is lowered by administration of glyceryl trinitrate or by haemorrhage the response is present and the minimal value obtainable is lowered. In normal men the drug causes increased blood flow to the extremities; in the supine position normal subjects show a minimal pressure response, but in hypertensive subjects fall is proportional to initial diastolic pressure. In all subjects the drug causes a postural hypotension, showing loss of vascular tone.

V. J. Woolley

2076. **Physiopathology of Traumatic Arterio-venous Fistulae in Man.** (La physio-pathologie circulatoire des fistules artério-veineuses traumatiques chez l'homme)
R. Charlier. *Acta cardiologica* [*Acta cardiol., Brux.*] **1**, 232–255, 1946. 62 refs.

By catheterization of the right auricle the author has studied the cardiovascular changes in 5 patients, aged 19, 20, 25, 35, and 36 years, with large traumatic arterio-venous aneurysms. In each, the fistula had been present for more than 1 year but under 2 years, and in none was there evidence of infection or heart failure.

His findings (mean values) showed slight increase in pulse rate (82), a fall in blood pressure, particularly in diastolic pressure (59 mm. Hg), a rise in central venous pressure (+2 mm. water; range −2 to +9·5 mm. water; normal −7 mm.), and increased cardiac and systolic output (12·7 litres per minute; normal 5·5).

Temporary occlusion lowered the pulse rate (64), raised the diastolic blood pressure (78), decreased the cardiac output (8·4), and lowered the central venous pressure to zero, while permanent surgical occlusion allowed the cardiovascular system to become completely normal again. In 3 cases tested, temporary occlusion following atropinization still caused slowing of the pulse and a fall in central venous pressure. These observations were further confirmed in experiments on dogs anaesthetized with chloral, with carotid, jugular, or femoral anastomoses. The arterial pressure remained constant in 2 dogs but, on closure of the fistula, the pulse accelerated and the central venous pressure rose. A similar result was noted following section of both vagi.

From the combined experiments the author concluded that the slight tachycardia was induced not only by arterial hypotension but also by the rise in central venous pressure (Bainbridge's reflex), that the afferent path of this reflex did not lie only in the vagus nerve, and that the bradycardia (Branham's phenomenon) after closure of the fistula was not exclusively of vagal origin.

W. T. Cooke

2077. **Clinical Studies of the Pharmacologic Effects of Tetraethyl Ammonium Chloride in Hypertensive Persons made in an Attempt to Select Patients Suitable for Lumbodorsal Sympathectomy and Ganglionectomy**
R. Birchall, R. D. Taylor, B. E. Lowenstein, and I. H. Page. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **213**, 572–578, May, 1947. 2 figs., 5 refs.

Sedatives such as "sodium amytal" have been used extensively in assessing the suitability of hypertensive patients for sympathectomy. Because these and other measures have proved singularly unsuccessful, the present study was undertaken to determine if the tetraethyl ammonium ion which has been reported to have a specific depressive effect on sympathetic ganglia would prove more helpful. The chloride salt was given to avoid the sedative effect of the more commonly used bromide.

Sixteen hypertensive patients—11 suffering from essential hypertension, 4 from malignant hypertension, and 1 from chronic nephritis—were investigated. The first 8 were given doses averaging 33 mg. (range from 25 to 51) per kilo body weight by intravenous infusion of a solution containing 100 to 150 mg. per ml. of saline, sterilized by Seitz filtration. Because of alarming reactions from this dosage the remaining 8 patients received only 4 to 7 mg. per kilo body weight in a single intravenous injection. In 14 of the 16 patients there was appreciable reduction in blood pressure following the injection; this began 1 minute after the injection, reached its maximum in 3 to 5 minutes, was sustained for 10 to 15 minutes, and gradually returned to the pre-injection level. Twelve patients had lumbodorsal sympathectomies, but in only 2 was there any significant change in the resting supine blood pressure 2 to 4 weeks after operation.

This paper emphasizes the unpleasant and often alarming side-effects of tetraethyl ammonium chloride; these increase in type and severity with the size of the dose. With the initial fall in arterial pressure, appeared mydriasis and cycloplegia, ptosis, numbness and tingling in the limbs and tongue with a metallic taste in the mouth; these symptoms were followed in about half the patients by dryness of the mouth, muscular weakness, and nasal congestion. Still later, in patients receiving large amounts of the drug, curariform effects occurred—dysarthria, dysphagia, and diaphragmatic paralysis with respiratory distress. One patient developed vasomotor collapse and became unconscious and apnoeic but recovered in 5 hours.

It is concluded that tetraethyl ammonium chloride has no highly selective depressive action on the sympathetic ganglia but that it affects also parasympathetic ganglia, and sensory and motor functions. Thus it is not surprising that, since the drug's effects on blood pressure

are due to a complex and diffuse action on many structures, the fall in arterial pressure following tetraethyl ammonium chloride bears no demonstrable relation to that following sympathectomy; hence it is valueless as a pre-operative guide in the selection of hypertensive patients for this operation.

[The data given in this paper throw considerable doubt on the earlier and extravagant claims made for tetraethyl ammonium salts in the treatment of peripheral vascular disease (Berry, Campbell, Lyons, Moe, and Sutler, *Surgery*, 1946, **20**, 525).] *Henry Cohen*

2078. **Potassium Thiocyanate in the Treatment of Hypertension**

G. WATKINSON and G. EVANS. *British Medical Journal* [*Brit. med. J.*] **1**, 595–598, May 3, 1947. 14 refs.

Briefly reviewing previous reports on the treatment of hypertension with thiocyanate, the authors consider that the results have been conflicting because of failure to recognize and differentiate the various arteriosclerotic processes underlying the hypertension, and because of the small difference between therapeutic and toxic levels of thiocyanate.

The methods used and the results obtained in 60 patients with hypertension are described. The authors recognized four clinical groups: (1) *Benign hypertension, quiescent phase* (23 cases). Blood pressure is consistently raised, but is not rising; diastolic pressure is below 130 mm. Hg. Retinal haemorrhages and haematuria are absent. (2) *Benign hypertension, active phase* (21 cases). Blood pressure fluctuates widely, and retinal haemorrhages and haematuria occur. (3) *Malignant hypertension* (10 cases). Greatly raised blood pressure, papilloedema, and retinal and renal haemorrhages are found. Evidence of renal failure exists. (4) *Renal hypertension* (6 cases).

All the patients received potassium thiocyanate in the doses necessary to maintain the blood level of thiocyanate at 5 to 12 mg. per 100 ml. Since the amounts necessary varied greatly in different patients, all received, after a control period in bed so that the effect of rest on the hypertension could be ascertained, 0·1 g. potassium thiocyanate three times a day for 1 week (a total dose of 2·1 g.). This was taken with food if symptoms of gastro-intestinal irritation ensued. The serum thiocyanate concentration was then estimated and the dose increased or decreased according to the value found—increased if the level was below 5 mg. per 100 ml. and decreased if it was above 7 mg. per 100 ml. Repeated estimations of serum thiocyanate were carried out weekly until the dose necessary to maintain the level between 5 and 7 mg. per 100 ml. for 3 successive weeks was found. Subsequent estimations were made at fortnightly or monthly intervals. Dosage should be based on repeated serum estimations and not upon the blood pressure, and the dose of potassium thiocyanate should not be increased by more than 0·4 g. in any 1 week.

The results of this treatment were assessed by the effects on symptoms and on blood pressure, the symptoms being recorded as cured, improved, or unaffected. The lowest blood pressure recorded during a preliminary control week in bed was taken as the base-line reading. The effect on blood pressure was considered significant if the average reading in the third week of treatment showed a fall from this base-line of 40 mm. Hg systolic and 20 mm. Hg diastolic. Late effects in 42 patients who received adequate doses of thiocyanate for 1 year or more are given. Of the 60 patients on whom the immediate effects are reported, 37 obtained symptomatic relief, and in 34 a "significant" fall in blood pressure occurred. Of the 42 patients who were followed up for a year or more 17 reported symptomatic relief and 18 a "significant" lowering in blood pressure. In all, 12 deaths occurred, 8 due to uraemia and 4 to coronary thrombosis. The most pronounced effect of the drug was in the relief of headache, dizziness, and vertigo; cardiac symptoms such as anginal pain and palpitations were not significantly effected.

The toxic effects are skin rashes, which may occur with low levels of thiocyanate, excessive tiredness, indigestion and nausea, thrombophlebitis, and goitre. In the present series 6 patients developed skin rashes and 2 thrombophlebitis. No other complications except gastro-intestinal symptoms were encountered, and this is attributed to the close control of the serum thiocyanate levels.

[No control series of cases given placebos is recorded. The results are considered to justify the differentiation of patients with hypertension into the four groups described. However, there is no statistical significance between the immediate results in any of the groups.] *G. A. Smart*

2079. **Peripheral Blood-flow in Rabbits with Experimental Hypertension.** [In English]

F. BÁRÁNY. *Acta Medica Scandinavica* [*Acta med. scand.*] **127**, 376–381, 1947. 1 fig., 12 refs.

2080. **Raynaud's Disease in Men**

D. I. ABRAMSON and H. B. SHUMACKER. *American Heart Journal* [*Amer. Heart J.*] **33**, 500–507, April, 1947. 2 figs., 8 refs.

Though it is generally believed that Raynaud's disease is a predominantly female complaint, 50 cases diagnosed as of Raynaud's disease were seen at the centre set up by the U.S. Army for the care of vascular disorders. The criteria for diagnosis were intermittent coldness with blanching or cyanosis of the digits precipitated by exposure to cold or emotion, and the absence of signs of organic vascular disease. The typical triphasic colour change of pallor, cyanosis, and redness in an attack was only seen in half the patients; nutritional changes of the fingers occurred in 8 cases. It is admitted that at least half the patients were not observed for over 2 years so that the presence of organic vascular disease could not be excluded. Patients with a history of local injury by freezing, cold, or mechanical trauma, or who had used vibrating tools, were excluded.

Sympathectomy was performed on 7 of the patients and the immediate results were satisfactory, though the operation is only recommended if conservative treatment fails. *H. E. Holling*

Disorders of the Blood

2081. **Heinz Bodies.** (Les corpuscles de Heinz)
M. A. GAJDOS. *Sang* [*Sang*] **18**, 30–35, 1947.

2082. **Biological Significance of Heinz Bodies. Their Relation to Verdoglobins.** (Signification biologique des corpuscles de Heinz. Leur rapport avec les verdoglobines)
M. A. GAJDOS and G. TIPREZ. *Sang* [*Sang*] **18**, 35–43, 1947. 4 figs., 7 refs.

Heinz bodies, small refractile granules in the surface layer of the red cell demonstrable only by supravital staining, are found in poisoning by hydrazines, aniline and its derivatives (including most sulphonamides), organic nitro-compounds, and sodium nitrate, and occasionally in malaria, chronic myeloid leukaemia, and after splenectomy for acholuric jaundice (Chauffard-Minkowski). *In vitro* they appear in blood preserved at 37° C. (but not at 0° C.) after 24 to 48 hours, but they appear within a few minutes if phenylhydrazine is added. The production of Heinz bodies *in vitro* by the action of hydrazines or cyanides at 37° C. depends also on the *p*H of the medium, none being formed at a *p*H below 6·6; nearly all cells contain them at *p*H greater than 7·0. Heinz bodies are also produced by the addition of ascorbic acid, the same conditions of temperature and *p*H being necessary; these bodies are, however, much smaller than those produced by the other reagents. All samples of blood containing numerous Heinz bodies show the spectrum of a verdoglobin (globin-verdohaemochromogen) when lysed. Verdoglobin is formed from haemoglobin *in vitro* under exactly the same conditions (nature of reagents, temperature, and *p*H) as are Heinz bodies. The authors conclude that the appearance of Heinz bodies depends on the scission of the porphyrin ring of haemoglobin to form globin-verdohaemochromogen, one source of the " readily split-off iron " and a stage in the formation of bilirubin. *G. Discombe*

2083. **The Transition Forms of Blood Groups**
L. HIRSZFELD. *Journal of Immunology* [*J. Immunol.*] **55**, 141–151, Feb., 1947. 3 figs., 5 refs.

A review of the author's theory of the antigenic structure of the A_1A_2BO blood groups is here presented in English; the work leading up to this theory has appeared during the last 10 years in Swiss, German, and French journals.

By parallel titrations of red cells of group A_1 against anti-O (goat anti-Shiga bacillus) and anti-A sera, several different forms can be separated. Some appear to have more O substance and less A substance and some the reverse, the total antigenic substance being constant. The reaction of A blood with anti-O serum does not depend on the blood being heterozygous O, for in testing a large number of samples of blood, many of which must have been A_1A_1 (18% in Poland), none was found which was completely negative with the anti-O serum. Further, the blood of known A_1A_1, A_1A_2, A_1A_2, and A_2B persons was agglutinated by the anti-O serum. The author therefore considers that the cause of the agglutinability " must be searched for in the structure of the A and B genes as such ".

The hypothesis is put forward that there is a range of increasingly complete mutations stretching from O through $A_5 \rightarrow A_4 \rightarrow A_3 \rightarrow A_2 \rightarrow A_m \rightarrow A_r \rightarrow A_j$ to A_c. A_5 is so weak in A that the cold agglutinin anti-A is present in the serum; A_4 is what is usually thought to be a group O with anti-A missing from its serum. The stages A_m, A_r, and A_j correspond to the classical A_1 gene, and the hypothetical A_c is completely A. The mutations appear to be changes of similar nature, but of increasing extent. A parallel series is proposed from O to B_c. People who possess anti-O are considered to be A_cA_c, A_cB_c, or B_cB_c. The rarity of persons of these groups explains the infrequency of anti-O.

[It is a pity that this very important paper is not more detailed; the conceptions of gene and genotype are not clearly distinguished, and from reading this paper alone one would be left wondering whether the bloods classified as A_m, A_r, and A_j were known AO heterozygotes, for, if they were not, it seems that A_mA_m might have as much A and O substance as A_jO, and be indistinguishable from it. This aspect is considered in *Ann. Inst. Pasteur*, 1940, **65**, 251 and 386. The author suggests that the direction of mutation is away from O towards A_c, and that O may eventually disappear. Such progressive evolution is not in accord with current doctrine. It also conflicts with Ford's view that the blood groups represent a balanced polymorphism (*Genetics for Medical Students*, 1942, p. 19). The evolutionary conjectures are not, however, as the author points out, an essential part of his theory. The theory does not seem capable of explaining the presence of α_1 in the serum of A_2B persons when this α_1 is active at body temperature. At least three such cases have been reported by experienced workers.]
R. R. Race

2084. **A Note on Studies of Hemolysis in Paroxysmal (Cold) Hemoglobinuria**
P. F. WAGLEY, W. H. ZINKHAM, and A. A. SIEBENS. *American Journal of Medicine* [*Amer. J. Med.*] **2**, 342–346, April, 1947. 2 figs., 11 refs.

Studies were made in the Johns Hopkins University School of Medicine on the mechanism of haemolysis in a male negro syphilitic patient who complained of abdominal pain and of passing dark urine after exposure to cold. He had a positive Donath-Landsteiner reaction. The conclusions reached are that: (1) under specified conditions the addition of carbon dioxide to the serum of a patient with paroxysmal haemoglobinuria will cause *in vitro* haemolysis, such haemolysis not being

due to a lowering of the *p*H such as occurs in nocturnal haemoglobinuria; (2) carbonic anhydrase inhibitors, such as sulphanilamide and cyanide, may in certain circumstances prevent the haemolysis; (3) definite morphological changes of the erythrocytes occur before haemolysis. *Geoffrey McComas*

2085. **A Factor in the Blood Serum Increasing Erythrocyte Respiration.** (Über einen die Erythrocytenatmung steigernden Faktor in Serum)
J. PIRWITZ. *Klinische Wochenschrift* [*Klin. Wschr.*] **24/25**, 263–265, Feb. 1, 1947. 4 figs., 23 refs.

The oxygen uptake of normal red cells suspended in serum is roughly proportional to the reticulocyte count of the blood from which the serum was obtained, irrespective of the cause of the reticulocytosis. Comparable changes occur with cells of leukaemic blood and of the bone marrow in haemolytic anaemia.

The author has previously observed that the injection into an anaemic subject of 50 ml. serum from blood showing a reticulocytosis of 5% or more will usually produce a definite reticulocyte response and a rise in haemoglobin of 10 to 15%; this fails to occur if the recipient is suffering from a severe toxaemia. Both observations are explained by the hypothesis that a substance stimulating the respiration and metabolism of red cells and their precursors is liberated into the blood at the same time as reticulocytes are released; there appears to be a humoral factor in blood regeneration. *G. Discombe*

2086. **Quantitative Cytologic Study of Multiple Sternal Marrow Samples Taken Simultaneously**
P. PIZZOLATO and J. STASNEY. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **32**, 741–748, June, 1947. 14 refs.

An attempt was made to find out how far samples of sternal marrow taken from different sites in the same patient differ from one another. Thirty patients with various diseases were examined. The sternal marrow was taken from sites 2 to 3 cm. apart; the nucleated cells were counted and the myeloid-erythroid proportion after centrifuging in a Wintrobe haematocrit tube was estimated. Differential counts were carried out on each sample. Comparison of the results often showed quite large differences on individual points, but the trend of cellular differentiation was always the same; for instance, if one sample showed predominance of erythroblastic proliferation, the second sample would show the same even though the figures were not identical. In hyperplastic marrow agreement was closer. In no case would a different report have been given on the two samples, and the authors conclude that " morphologic or pathologic appraisal of any one region of the marrow will usually reveal trends in other portions of marrow throughout the body ". *M. C. G. Israëls*

2087. **Diagnosis of Anemias in Infancy and Childhood**
C. H. SMITH. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **134**, 992–997, July 19, 1947. 1 fig., 9 refs.

2088. **Our Present Knowledge of Icterus with Anaemia, Micropoikilocytosis and Increased Red Cell Resistance. (Rietti-Greppi-Micheli Syndrome).** (Le nostre conoscenze attuali sull'itteroanemia con micropoichilocitosi ed aumento della resistenza globulare tipo Rietti-Greppi-Micheli)
P. FORNARA. *Gazzetta Medica Italiana* [*Gazz. med. ital.*] **56**, 69–83, April, 1947.

2089. **Clinical Features of Rietti-Greppi-Micheli's Syndrome.** (Il quadro clinico della malattia di Rietti-Greppi-Micheli)
F. TOSCANO. *Gazzetta Medica Italiana* [*Gazz. med. ital.*] **56**, 83–88, April, 1947.

2090. **The Bone Marrow and Myelopathic Factors in the Ictero-anaemic Syndrome.** (Il midollo osseo ed i fattori mielopatici nella sindrome anemico-itterica di Rietti-Greppi-Micheli)
A. MARMONT. *Gazzetta Medica Italiana* [*Gazz. med. ital.*] **56**, 88–95, April, 1947. 5 figs., 1 ref.

2091. **Therapeutic Possibilities in the Ictero-anaemic Syndrome.** (Le possibilità terapeutiche della sindrome anemicoitterica di Rietti-Greppi-Micheli)
G. BARENGHI. *Gazzetta Medica Italiana* [*Gazz. med. ital.*] **56**, 95–99, April, 1947.

2092. **Considerations on Haemolytic Icterus with Increased Red Cell Resistance.** (Considerazioni sull'ittero emolitico con resistenze globulari aumentate tipo Rietti-Greppi-Micheli)
P. FORNARA. *Gazzetta Medica Italiana* [*Gazz. med. ital.*] **56**, 100–101, April, 1947.

This symposium on Mediterranean anaemia by four Italian experts is especially valuable as a key to the European literature on the subject. The limited geographical distribution of the disease, even within Italy, is emphasized. The disease is seen in the southern half of the peninsula and in Sardinia, but is rarely observed in the northern plains. The distribution is very similar to that of malaria, and a possible relation thereto is discussed. The clinical and haematological observations contain little that has not been described by American and British authors. *G. Discombe*

2093. **Experimental Study of Haemolytic Icterus by Injection and Ingestion of Antiserum.** (Études sur l'ictère hémolytique expérimental par injection et ingestion d'antisérum)
M. BESSIS. *Revue d'Hématologie* [*Rev. Hématol.*] **2**, 114–146, 1947. 20 figs., 13 refs.

Dameshek and Schwartz produced in guinea-pigs various syndromes of haemolytic anaemia by the injection of rabbit anti-guinea-pig serum, and suggested that in man many haemolytic anaemias were due to auto-antibodies. The present author, starting with the knowledge that haemolytic anaemia of the newborn is due to destruction of red cells by iso-antibodies from the mother, has repeated the experiments of Dameshek and Schwartz on albino rats, aged from 1 day to 4 months,

using rabbit anti-rat serum. The prepared anti-rat serum was titrated for agglutinin and haemolysin content. It was administered to the rats in arbitrary units by intramuscular, intraperitoneal, subcutaneous, and oral routes. Control rats given normal rabbit serum and anti-rat rabbit serum absorbed *in vitro* with rat red cells showed no abnormalities.

The young rats given large doses (35 to 120 units per g.) of anti-rat serum developed haemoglobinuria and died. After doses of the order of 15 to 30 units per g., the rats developed pallor, icterus, urobilinuria, and splenomegaly. Death usually occurred after about 24 hours. Small doses, less than 5 units per g., produced pallor and sometimes slight icterus, but the animals recovered. Examination of the blood of these rats showed absence of normal rouleaux formation, but the presence of red cells in chains like streptococci, extremely deformed red cells probably as a preliminary state to spherocytosis, and clumping of spherocytic forms. Crystals of haemoglobin appeared within some of the red cells; these were observed extracellularly when these red cells ruptured. Primitive red cells were seen in considerable numbers. Marked leucocytosis occurred, often with the appearance of large numbers of erythrophagocytic monocytes. Histologically the tissues were similar to those in cases of haemolytic anaemia of the newborn. However, erythrophagocytic cells were very numerous in the tissues; gross changes in hepatic cells and biliary thrombi were not seen, nor were cerebral lesions. Sensitization of the recipient rat's red cells was demonstrated serologically by the conglutination reaction; free antibody was present in the serum. Rats up to 20 days old when given anti-serum by mouth showed the same syndromes.

The author's conclusions were that most of the phenomena of haemolytic disease of the newborn had been reproduced experimentally, though fulminating haemolytic anaemia, such as could be produced artifically, did not occur naturally, and cytotoxic effects which are seen in the naturally occurring disease were not observed in this trial. *John F. Loutit*

2094. **On the Curative Effect of Pure Duodenal Secretion from Swine in Cases of Pernicious Anemia.** [In English] E. LANDBOE-CHRISTENSEN and C. L. S. BOHN. *Acta Medica Scandinavica* [*Acta med. scand.*] **127**, 116–129, March 22, 1947. 4 figs., 23 refs.

Samples of duodenal secretion free from gastric or pancreatic secretion and from bile were obtained from swine in which the gut had been divided and ligated just proximal to the opening of the bile duct and also just proximal to the opening of the pancreatic duct. Cholecysto-gastrostomy and posterior gastro-jejunostomy were then performed, and a tube was sutured into the pouch of duodenum thus formed. After the experiment was completed necropsy revealed that this duodenal pouch had no connexion with any other part of the alimentary tract.

To a patient aged 41 years, with all the classical haematological changes of pernicious anaemia, including a megaloblastic marrow, 150 ml. duodenal secretion was given daily for 10 days. A reticulocyte response of 8·4% was obtained on the seventh day, and no further response was obtained when an active liver extract was given parenterally; the megaloblastic marrow had become normoblastic. Another patient, aged 83, with a red cell count of 3,000,000 per c.mm., gave no response either with duodenal juice or with parenteral liver extract.

The authors consider that the differences between their results and those of Castle, Townsend, and Heath (*Amer. J. med. Sci.*, 1930, **180**, 305) with human duodenal secretion may be due to the fact that their dosage appears to have been about ten times larger than that used by Castle *et al.*, though it is possible that duodenal juice of human subjects is inactive. *G. Discombe*

2095. **Experimental Study of Leukaemias and Tumours of the Reticulo-endothelial System.** (Recherches expérimentales sur les leucémies et les tumeurs du système réticulo-endothélial)
M. GUÉRIN. *Revue d'Hématologie* [*Rev. Hématol.*] **2**, 13–36, 1947. 6 figs., 37 refs.

This article is a summary of work done at the Institut du Cancer over the last 15 years.

The carcinogenetic action of leukaemia virus was studied. A strain of avian erythroblastic leukaemia provided the virus. Attempts to fix the virus to cells of the reticulo-endothelial system were successful only when the virus itself rather than the recipient animal was treated. With refrigerated storage and glycerin treatment of the infected blood or organs sarcomata were often produced within 1 to 4 months, particularly at the site of inoculation. Some of these metastasized. Transplants of these tumours produced lesions ranging from reticuloses to sarcomata. A sarcoma was also produced from a Chamberland filtrate, proving the sarcomatogenic power of the virus itself. Other strains of leukaemia virus have been shown to be similarly active. Evidence is presented that the tumorigenic and leukaemic properties are due to the same virus.

Passive immunization did not protect fowls subsequently inoculated with leukaemic blood. Attenuation of the virus before inoculation caused some slight immunity. However, better results were obtained by injections of fresh blood diluted 10,000, 1,000, and 100 times or of preserved blood undiluted or diluted 10 or 100 times. Formolization of blood diluted 300 times appeared to give better results still.

Quinine and "plasmoquine" were without effect in treatment; rhodoquine appeared to be partially effective.

Leukaemia and myelosarcoma in rats were rare and only two chloroleukaemias were transplantable. Tumours developed at the site of injection, metastasized and finally a leukaemic reaction was noted in the blood. Protoporphyrin was found in the tumours.

Spontaneous lymphosarcomata were rare in rats and affected mesenteric lymph nodes. They were of varying histological types. Only the lymphocytic form was associated with leukaemoid reaction. A lymphoblastic form was transplantable.

Reticulo-endothelioses were found in the mouse, both as diffuse lesions of inflammatory type and as nodular

areas of a neoplastic character. Blood from a human case of reticulo-endotheliosis inoculated into mice produced in some animals a paraplegia, in others an abdominal syndrome of reticulo-endotheliosis. Livers from mice affected with spontaneous reticulo-endotheliosis carried a transmissible and filter-passing agent. Work has also been done on tumours induced with benzpyrene. *John F. Loutit*

2096. **Thiouracil in the Treatment of Leukemia**
O. C. HANSEN-PRUSS. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **64**, 496–500, April, 1947. 4 refs.

Thiouracil was administered to 6 patients with chronic myelogenous leukemia, and to 1 patient with an acute myeloblastic leukemia. The dosage averaged 1·5 g. a day and was well tolerated by every patient. One patient received a total of 395·3 g. of the drug over a 10-month period. The drug had no effect on the total circulating white count, nor on the differential white cell picture, red cell elements, haemoglobin or platelet values, or the bone marrow pattern.

Thiouracil did not influence the metabolic rate of leukaemic patients materially when given in a dose of 1·5 g. daily. This was true whether it was administered over a period of 2 weeks, 2 months, or 10 months. The serum cholesterol rose in only 2 patients, and this rise was only transitory. In 1 patient the serum cholesterol continued to fall, the basal rate steadily rose despite the administration of thiouracil. In 1 patient reported, and in 2 others this drug failed to prolong or modify the remission induced by irradiation. Thiouracil given in the dosage reported in this series had no demonstrable effect on the myeloid dysfunction, basal metabolic rate, the serum cholesterol level, or the bone marrow pattern of patients with myelogenous leukaemia.

Thiouracil, furthermore, did not modify the clinical course of the disease. It seems certain, therefore, that this drug has no value as an adjunct in the treatment of myelogenous leukaemia.—[From the author's conclusions.]

2097. **Familial Leukemia. A Preliminary Report.** [In English]
A. VIDEBÆK. *Acta Medica Scandinavica* [*Acta med. scand.*] **127**, 26–52, March 22, 1947. 1 fig., Bibliography.

The author reviews 26 families, in each of which 2 or more members had leukaemia, together with 56 families in which the evidence is suggestive but not conclusive. He records his own investigation of the families of 211 patients with leukaemia, finding 16 proved cases and 1 doubtful case in 12 families with more than 1 leukaemic patient. The incidence of the different types of leukaemia in the familial cases was compared with that in 310 cases observed during the last 10 years in the Copenhagen hospitals; there was no significant difference. The age of onset was slightly less in the familial cases than in the unselected series.

[This is a most complete review of the literature, which should be read in the original by those interested.]
G. Discombe

2098. **Leukaemia as a Neoplastic Disease.** (Bialaczka jako choroba nowotworowa)
A. BIERNACKI. *Polski Tygodnik Lekarski* [*Polsk. Tyg. lek.*] **2**, 443–448, April, 1947. 47 refs.

The aetiology of leukaemias still remains obscure and in the author's opinion neither Naegeli's endocrine theory nor the infection theory can be substantiated. There are several observations which support the view that leukaemia is a neoplastic disease. The fact that no primary neoplastic lesion has been found in leukaemia should not be over-emphasized, since several tumours are known to originate in multiple foci (neurofibromata, gliomata, endotheliomata). On the other hand, cases are known where leukaemic changes localized to the bone marrow have preceded the infiltration of other organs. The resemblance to neoplastic cells can be seen in the poor differentiation of white blood cells, the variety of paramyeloblastic cells and the morphology of their nuclei. The author quotes cases in which tumour-like growths have been the outstanding signs of leukaemia. He describes 2 more cases of this type. One patient had a tumour in the left supraclavicular region causing symptoms of tracheal compression. Exploratory excision suggested the diagnosis of lymphosarcoma, but soon afterwards the patient developed an acute leukaemia and died. Necropsy confirmed the diagnosis of leukaemia. The second case was one of retrosternal chloroma, and necropsy revealed typical leukaemic infiltrations. The fact that leukaemia is more common in those who work with *x* rays, radium, benzol, and other growth-stimulating agencies also supports the neoplastic aetiology of leukaemia. In the author's view acute leukaemia is a malignant neoplasm and chronic leukaemia a benign neoplasm which gradually becomes malignant and leads to a fatal termination. *J. T. Leyberg*

2099. **Myelosclerosis with Leukoerythroblastic Anemia**
M. L. SUSSMAN. *American Journal of Roentgenology and Radium Therapy* [*Amer. J. Roentgenol.*] **57**, 313–320, March, 1947. 11 figs., 6 refs.

The author gives a brief history of the clinical features, blood and bone-marrow examinations, and some post-mortem findings in 9 patients, male and female, of varying ages from 42 to 67 years, who presented radiographic evidence of sclerotic changes in the bones in association with extramedullary haematopoiesis.

The changes in the peripheral blood during life and in the viscera and bones at necropsy are variable but resembled those of chronic myelogenous leukaemia, though the clinical history is atypical. There is marked extramedullary haematopoiesis, which is in excess of what could be expected from the degree of marrow replacement, and there is a leucoblastic invasion of many organs. In certain cases there is an increase for several years in the number of cells of the erythrocyte series as well as in the relative number of immature cells of this type, but without a reduction in the other marrow elements. Some patients had a preceding polycythaemia vera for upwards of 20 years before the myelosclerosis and anaemia were recognized. The evidence of abnormal

stimulation may develop in the course of the disease, though the blood picture had previously been normal. The leucoblastic activity is likely to increase progressively, and many cases which appear to represent the "spent" phase of polycythaemia progress to what pathologists call, on the grounds of malignant invasion of the organs, myelogenous leukaemia, but the clinical course is atypical, and stimulation is not limited to a single cell type. The blood picture may be altered by irradiation and other therapeutic measures.

Associated with the myelosclerosis there is usually an increase in megakaryocytes in the bone marrow and an increase in the platelets; the term megakaryocytic anaemia has been used. The cause of the medullary fibrosis is unknown. Whatever the onset, the anaemia and leucoblastic activity in most cases finally become progressive and ultimately death occurs with leukaemic invasion of the spleen and other organs. The osteomyelosclerosis causes a typical change in the radiographic appearance of the bones of the skeleton. They become abnormally dense, often showing on superficial examination a normal relation of cortex and medulla. They remain unchanged, however, in shape and peripheral regularity, so that apart from their typical clinical features, cases can be distinguished from other conditions associated with abnormal density of the bones, such as Albers-Schönberg disease, fluorosis of bone, Paget's disease, and prostatic and other carcinomatosis of bone. It is in the texture of the bone that the change is seen; the cancellous tissue, which at first may appear coarser, gradually becomes granular or obliterated by the deposition of new bone, giving it its greater density. At necropsy, such bones will be found to be abnormally heavy owing to the increased density of the changed marrow. *James F. Brailsford*

2100. **Giant Follicular Lymphoblastoma (Brill-Symmers' Disease)**

J. F. PANTRIDGE. *Ulster Medical Journal* [*Ulster med. J.*] **16**, 46–53, May, 1947. 8 figs., 8 refs.

This is an account of 7 cases of giant follicular lymphoblastoma. The author considers that the disease is little less than half as common as lymphosarcoma, and that some 27% of lymphosarcomata arise from a preceding follicular lymphoblastoma. It is thought that many cases of lymphoblastoma are unrecognized because early sarcomatous change completely obscures the hyperplastic process.

In treatment it must be remembered, first, that sarcomatous change may occur while the condition is still localized to one group of lymph nodes; and secondly, uncomplicated follicular lymphoblastoma is usually amenable to mild *x*-ray therapy. In order that sarcomatous change may be prevented or delayed biopsy should be performed early in patients with localized or generalized lymphadenopathy of doubtful origin and localized giant follicular lymphoblastoma should be treated by removal of the affected nodes; deep *x*-ray therapy should be given for the general condition.

R. B. Lucas

2101. **Nitrogen Mustards in Hodgkin's Disease. Report on 21 Cases and 4 of Other Reticuloses**

M. I. R. APTHOMAS and H. CULLUMBINE. *Lancet* [*Lancet*] **1**, 899–901, June 28, 1947. 3 figs., 6 refs.

The use of nitrogen mustards is described in the treatment of 21 cases of proved Hodgkin's disease in an advanced stage, 2 cases of lymphosarcoma, 1 case of reticulum-celled sarcoma, and 1 case of mycosis fungoides. There are two forms of nitrogen mustard: (1) tris-β-chloroethylamine hydrochloride ("tris" form), (2) methyl-bis-β-chloroethylamine hydrochloride ("bis" form).

The bis form was used first, the dose being dissolved in 10 to 20 ml. of saline and injected intravenously. The usual dose in the first course of treatment was 0·4 mg. per kilo body weight. The first patients were given an injection of 0·1 mg. per kilo body weight on 4 consecutive days; later, two injections, each of 0·2 mg. per kilo, at 24-hour intervals were given. The period of vomiting was shorter with the latter technique. A few patients were treated by intravenous drip, each dose being dissolved in 500 ml. saline, but this method did not lessen local thrombosis. Courses were repeated after an interval of 6 to 8 weeks, the dosage being increased to 0·3 mg. per kilo body weight on each of 2 successive days. Two patients received four daily injections of 0·2 mg. per kilo, but this dosage led to a severe leucopenia.

Nausea and vomiting occurred in all cases except 1, lasted for 24 to 48 hours, and continued for longer after the tris than after the bis form. Thrombosis at the site of injection was noted in 6 patients. The most important toxic effect was leucopenia, usually within 3 to 21 days of treatment. Neutrophils were particularly affected. In 5 patients the white cell count fell below 1,000 per c.mm.; 2 of these had received double the usual dose of bis compound; the other 3 had the usual dose of the tris compound, and in them the leucopenia was accompanied by anaemia, thrombocytopenia, stomatitis, and petechial haemorrhages.

The results were satisfactory over the period of observation, which varied from 3 to 8 months. There was a striking improvement in the patient's general condition, the temperature usually becoming normal within 24 hours, lassitude disappearing, and weight increasing. Enlarged cervical and mediastinal nodes and spleen were reduced in size. All the 21 patients improved after the first course. Of the 13 patients who had two courses, 12 showed improvement after the second course; of the 4 who had three courses, only 2 were improved. It is thus possible that the disease gradually becomes more resistant to the drug. There was improvement in 1 of the 2 cases of lymphosarcoma, but no response in the cases of reticulum-celled sarcoma and of mycosis fungoides.

Radiotherapy is to be preferred as a first treatment in Hodgkin's disease for the following reasons: (1) the mean period of remission after radiotherapy is longer; (2) vomiting is less troublesome; (3) leucopenia is certain and sometimes severe after nitrogen mustard therapy. The tris form of the drug shows no advantages over the bis form, and the former is the more toxic.

Geoffrey McComas

Respiratory Disorders

2102. **Hemolytic Streptococcic Sore Throat. The Post-streptococcic State**
L. A. RANTZ, P. J. BOISVERT, and W. N. SPINK. *Archives of Internal Medicine* [*Arch. intern. Med.*] **79**, 401–435, April, 1947. 13 figs., 21 refs.

After haemolytic streptococcal infection certain non-suppurative complications may arise, alone or in various combinations, such as arthritis, late fever, carditis, late lymphadenitis, pneumonia, a persistently rapid erythrocyte sedimentation rate, purpura, glomerulonephritis, and prolonged initial fever. All these disorders are believed to be manifestations of the same pathological process, and it is suggested that they may be caused by an immunological reaction in persons whose tissues have been sensitized to the haemolytic streptococcus by previous infection. These disorders are regarded as phases of the "post-streptococcic state". In the present study detailed investigations were carried out in military personnel discovered to be suffering from infection with haemolytic streptococci. The organisms were identified serologically by the precipitin techniques of Lancefield, and serial white cell counts, erythrocyte sedimentation rates (E.S.R.), and electrocardiograms were obtained. Examples of sore throat caused by group A haemolytic streptococci, with and without rash, were studied. Of 299 cases 72 were regarded as possible examples of the post-streptococcic state. Infection by group A haemolytic streptococci was positively established in all these cases by the presence of rash or a significant antistreptolysin or antifibrinolysin response.

Arthritis occurred in 19 cases and, when associated with fever and carditis, was indistinguishable from classic rheumatic fever. A true "latent period" between the initial throat infection and this complication was only occasionally seen, usually with abnormal electrocardiograms or raised E.S.R. Seven patients remained afebrile and pyrexia was generally terminated by salicylates. There was electrocardiographic evidence of carditis in 9 cases, but valvular disease did not develop during the period of study. Cardiac involvement was more likely to occur in febrile patients. The E.S.R. was invariably rapid. No serological type of organism was more likely than others to initiate arthritis. There was reinfection by new types in 5 of these cases. Late fever, persisting from 2 to more than 40 days, occurred in 14 patients, and was associated in 13 cases with a raised E.S.R. which often persisted for several weeks. Electrocardiographic, but not clinical, evidence of carditis was obtained in 5 of the cases. Late fever appeared earlier and was less severe and of shorter duration than fever in the arthritic cases. Electrocardiographic evidence of carditis was obtained in 11 patients convalescent from haemolytic streptococcal sore throat in whom no other disorder was present. In all of these the E.S.R. was elevated, but there was no clinical evidence of carditis. There were 8 cases of late lymphadenitis, 7 cervical and 1 probably abdominal. This complication differed from the others in that there was no evidence of carditis in any of the cases and the E.S.R. was normal in 4. Radiological evidence of patchy pneumonitis was present in 3 cases associated with post-streptococcal fever. Pneumococci were absent from the sputum, and there were only small numbers of haemolytic streptococci. Recovery without chemotherapy was rapid. Arthritis accompanied by carditis developed in 1 case. Leucocytosis was present in all cases. For these reasons the pneumonitis was considered to be a post-streptococcal non-suppurative complication. The E.S.R. remained abnormally rapid for more than 3 weeks in 10 cases without obvious cause. Electrocardiograms were normal. There were 2 cases of non-thrombopenic purpura, in neither of which could sulphonamides or some unknown toxic agent be excluded as possible aetiological factors. Prolonged initial fever of 10 or more days' duration accompanied the initial throat infection in 5 cases, in 4 of which the electrocardiogram was abnormal.

The development of late non-suppurative complications was not prevented by treatment of the initial sore throat with large amounts of sodium salicylate, with a short course of penicillin alone or followed by sulphadiazine, or with the latter drug alone. In a group of 13 cases given 500,000 to 1,000,000 units of penicillin in 80 hours, post-streptococcal disorders did not develop. The authors rightly refuse to draw conclusions in view of the small number of patients so treated.

[Much valuable information is presented in this lengthy paper, which should be consulted by all those interested in the subject. The authors' work on the chemotherapy of the initial haemolytic streptococcal throat infection in relation to the development of "rheumatic" complications merits repetition on a large scale. The importance of preventing such complications requires no emphasis.]

J. L. Markson

2103. **Respiratory Motor Phenomena of Conversion Hysteria**
I. M. ALLEN. *New Zealand Medical Journal* [*N.Z. med. J.*] **46**, 113–122, April, 1947. 24 refs.

Contraction or impaired relaxation of antagonistic muscles and inhibition of the motor impulse to the affected muscles are factors concerned in the production of hysterical loss of power. Similarly, dyspnoea may be produced by incoordination of action of the diaphragm, abdominal wall, and intercostal muscles. In the "effort syndrome" type of breathlessness, it is mainly inspiration which is at fault, with inhibition of the motor impulse to the diaphragm, contraction of the anterior abdominal wall and chest wall, and inversion of the order of the movements involved in inspiration. In persons with this

kind of breathlessness the symptom may be provoked by applying firm pressure with the hand on the epigastrium at the start of inspiration; breathing is rapid and shallow and the patient becomes distressed and dyspnoeic with tachycardia, blurred consciousness, and tetanoid contractions of the hands. When, at any stage, pressure is released from the upper part of the abdominal wall the sequence of events is interrupted at once and breathing becomes normal. Patients taught to relax the upper part of the abdominal wall deliberately may be able to prevent the spontaneous development of such an attack.

Symptoms, depending upon lack of control of expiration, include stammering, spasmodic cough, sometimes expiratory stridor, and a clinical picture indistinguishable from bronchial asthma.

[This article helps to explain the beneficial effects of breathing exercises on patients with effort syndrome, asthma, and stammer.] *T. Semple*

2104. ***para*-Aminobenzoic Acid in Dyspnoea.. (Mode of Administration and Dosages.)** (L'acide *para*-aminobenzoïque dans les dyspnées. (Modes d'administration et posologie))

R. Benda, G. Poirot, M. Pernelie, and R. Wattebled. *Bulletins et Mémoires de la Société Médicale des Hôpitaux de Paris* [*Bull. Soc. méd. Hôp. Paris*] **63**, 445–449, May 30 and June 6, 1947. 10 refs.

The authors recommend the symptomatic treatment of dyspnoea of whatever origin with *para*-aminobenzoic acid. A 5% solution of its sodium salt was used at a *p*H of 7·0, 10 ml. being given slowly intravenously in the course of 1 to 2 minutes once a day; if necessary, intramuscular injections of the same quantity of the same solution were given in addition two to five times a day according to the effect. Except for a slight rise in temperature in 2 cases no untoward effects were observed among several thousands of such injections. Favourable effects were obtained in 24 of 34 cases of asthma; of 26 cases of dyspnoea of varied origin (tuberculosis, pyopneumothorax, carcinoma of bronchus, Hodgkin's disease) the results were good in 19. In some cases relief of dyspnoea was immediate and lasting after the first injection; in others only a partial and transient improvement resulted, so that injection had to be repeated. The same compound was also used in the form of aerosols. With tuberculous cavities with artificial pneumothorax or after division of adhesions, and in certain cases of residual cavities after extrapleural pneumothorax, intrapleural injections were given, combined with intravenous ones. This combination is claimed to give even more reliable results in such cases, but it is conceded that the cavities might have healed after division of adhesions without the drug treatment; no controls were available for comparison. *A. Schott*

2105. **The Significance of Bronchial Lesions in Pneumoconiotic Patients.** (Importance des lesions bronchiques chez les pneumokoniotiques)

W. Bruninx. *Acta Clinica Belgica* [*Acta clin. belg.*] **1**, 536–545, Nov.–Dec., 1946. 6 figs., 4 refs.

LUNGS

2106. **Symptomless Pulmonary Abscess.** (O ropniu płuc przebiegejacym bezobjawowo)

K. Kosieradzki. *Polski Tygodnik Lekarski* [*Polsk. Tyg. lek.*] **2**, 479–482, April 14–28, 1947.

This analysis of 114 cases of pulmonary abscess indicates that the typical syndrome is not always present, since 22·2% of the acute cases showed only a slight rise in temperature, and in 39·2% of the patients, whose illness had lasted more than 8 weeks, there was no rise in temperature. The white-cell count may also be misleading. In the acute cases 19·3% had a leucocytosis below 8,000, and 8·8% below 6,000. In chronic cases the leucocytosis was even less marked; the leucocyte count was less than 8,000 in 30·4% and less than 6,000 in 13%. Physical examination of the chest was often negative. In 16% of cases the amount of sputum was not increased and in some of them the sputum was not offensive. The final diagnosis must rely on repeated *x*-ray examination, but even so the differential diagnosis may prove difficult.

The author describes a case of bilateral bronchopneumonia in the course of which an abscess formed without any noticeable symptoms. Radiographs taken on the twenty-first day of illness revealed for the first time a well-marked abscess in the right upper lobe; a spontaneous evacuation of pus occurred within 5 days without an increase in sputum. During the formation of the abscess the temperature was falling, the leucocytosis decreasing, and the sedimentation rate falling from 80 mm. to 45 mm. Latent pulmonary abscesses probably form more frequently than is generally realized. *J. T. Leyberg*

2107. **Association of Pneumonia with Erythema Multiforme Exudativum**

J. H. Dingle, T. J. Abernethy, G. F. Badger, J. W. Beard, N. L. Cressy, A. E. Feller, I. Gordon, A. D. Langmuir, C. H. Rammelkamp, E. Strauss, and H. Tatlock. *Archives of Internal Medicine* [*Arch. intern. Med.*] **78**, 687–710, Dec., 1946. 8 figs., 46 refs.

The severe form of exudative erythema multiforme (Hebra) is a distinct clinical entity in which the mucosae of mouth, eyes, and urethra are predominantly involved. It is much less common than the benign manifestation. [This condition has received considerable publicity lately in the British medical press under the name of Stevens-Johnson syndrome. Other synonyms are: ulcero-membranous stomatitis, dermato-stomatitis, muco-cutaneous fever, ectodermosis erosiva pluriorificialis.]

In 3 of the 6 cases described by the present authors there was a non-bacterial pneumonia, which appeared to be an integral feature of the disease. [In 1 of the 2 cases of Stevens and Johnson there was a pneumonia of the right lower lobe, and pneumonia in association with the muco-cutaneous lesions has been reported several times, but its importance as an essential feature of the disease has not been emphasized.]

The skin lesions were erythemato-papular and vesicular or bullous, the former frequently in the shape of

erythema iris. The more bullous the rash, the greater the fever and constitutional disturbance and the extent of mucosal involvement. The superficial ulcers in the mouth became covered with a white membrane but eventually healed without scarring. Conjunctivitis was usually catarrhal, but if purulent might lead to scarring and even perforation of the cornea. Other regions frequently involved included the nares and nasal mucosa, lips, urethral meatus, glans penis, anus, vulva, and vagina. Prodromal symptoms suggestive of respiratory infection preceded the enanthemata by several days. Lesions first appeared in the mouth and conjunctivae; nasal and penile lesions followed, and the skin eruption was often the last manifestation and might continue to appear for 1 to 4 weeks. Apart from pulmonary involvement visceral lesions probably do not occur. There are no blood changes. Periarticular swelling has been described, but not synovial effusion. Differential diagnosis is from pemphigus, chickenpox, generalized vaccinia, human foot-and-mouth disease, and certain drug rashes. Buccal lesions may simulate herpetic gingivo-stomatitis or Vincent's stomatitis. Attempts to transmit an infectious agent to laboratory animals were unsuccessful.

It is stressed that pneumonia is an essential feature of the disease. The pharynx, epiglottis, vocal cords, and trachea are often involved by the typical enanthema, but the cause of the broncho-pulmonary lesions is not clear. The pneumonia may be caused by desquamation of the epithelium of bronchioles and alveoli with respiratory obstruction, but in many of its features bears a close resemblance to primary atypical pneumonia. This is shown especially by the prodromal symptoms, absence of physical signs of consolidation, minimal respiratory distress, absence of pleural pain or blood-stained sputum, relatively normal leucocyte count, and similar radiographic appearance. Two of the 3 cases were tested for cold agglutinins and both were positive; the test was performed in 2 of the 3 cases without pneumonia and in both was negative. Although unable to incriminate any known agent, the authors consider that the cause, at least of the pneumonia, is almost certainly a virus.

E. G. Sita-Lumsden

2108. **Roentgen Findings on Torulosis. Report of Four Cases**

R. R. GREENING and L. J. MENVILLE. *Radiology* [*Radiology*] **48**, 381–388, April, 1947. 5 figs., 59 refs.

Torula histolytica is an organism of the yeast group which rarely causes infection in man. Generally the central nervous system is involved and sometimes the lungs, more rarely the lungs alone. The authors have found 4 proved cases among half-a-million admissions over 10 years. In 3 of these there was pulmonary involvement. They report a total of 107 cases in the literature.

Symptoms are those of meningeal irritation with low-grade fever. When the lung is involved there are bronchitic symptoms with small amounts of sputum. The lesions in the lung take the form of patches of pneumonitis, which may coalesce, break down, and become secondarily infected. Characteristically the lesions are found at or near the lung bases and are seen as fairly well circumscribed opacities which grow and may become confluent. After healing, patches of fibrosis may remain. There may be a resemblance to tuberculosis but the site and the clinical features should help to differentiate the disease.

The 4 cases are reported in detail, with reproduction of the chest radiographs in the 3 cases with pulmonary involvement.

A. M. Rackow

2109. **So-called Pulmonary Adenomatosis and Alveolar Cell Tumours. Report of a Case**

M. A. SIMON. *American Journal of Pathology* [*Amer. J. Path.*] **23**, 413–427, May, 1947. 6 figs., 27 refs.

A clinical diagnosis of pneumonitis and pleural effusion had been made in the case of a woman, aged 70, who had had a history of cough and dyspnoea for 7 weeks. Necropsy revealed bilateral pneumonia-like consolidation, microscopical study of which, however, showed a widespread intra-alveolar tumour of glandular structure. [The author regards this as "arising from alveolar lining cells", but the mucus-secreting nature of the epithelium recalls that of many bronchial carcinomata, and in the abstracter's opinion the possibility of diffuse extension from an inconspicuous primary bronchial focus cannot be excluded.]

R. A. Willis

2110. **Bronchiogenic Carcinoma; An Analysis of 343 Cases**

R. K. HOLLINGSWORTH. *Annals of Internal Medicine* [*Ann. intern. Med.*] **26**, 377–385, March, 1947. 9 refs.

The significant point in this analysis of 231 histologically proven cases of bronchial carcinoma studied over a period of 6 years was not the patient's own delay in seeking medical advice when suffering from definite breathing disorders, but the slow progress made by clinicians in arriving at a positive diagnosis. In more than half the series it took at least 6 months for presumably well-equipped staff to make an accurate diagnosis. In all cases in which ordinary clinical and other examinations give rise to a suspicion of carcinoma of a bronchus the author relies upon bronchoscopy as a diagnostic procedure, as a guide to what is therapeutically practical, and as a basis for prognosis. But he also strongly advises exploratory thoracotomy in still doubtful cases.

The account given of the clinical features of bronchial carcinoma conforms to what is generally known and accepted in Britain. There is sound statistical evidence of the increasing prevalence of the malady. For clinical study the author brings in 112 additional cases of bronchial carcinoma not histologically proven and for some reason or other not radically treated.

A wide resection of diseased lung, together with the regional lymph nodes, is held to be the only practical worth-while measure but, even so, the prognosis is poor. Of the author's 231 patients only 77 were deemed operable, and of these only 43 were fit for a radical resection. Seventeen survived up to 3 years and 13 up to 7 years.

G. F. Walker

Digestive Disorders

STOMACH

2111. **A Preliminary Report on Protein Hydrolysate Therapy for Peptic Ulcer**
S. T. KIMBLE. *Gastroenterology* [*Gastroenterology*] **8**, 467–475, April, 1947. 5 refs.

Following Co Tui's report on the value of protein hydrolysate in the treatment of peptic ulcer, the authors treated 11 cases of duodenal ulcer, 1 of gastric ulcer, and 1 of combined duodenal and gastric ulcer with intragastric drip or intravenous administration of this substance. It is a heat-sterilized derivative of beef, containing 6% of amino-acids and polypeptides. Those patients treated with intragastric drip received 500 ml. of hydrolysate (25 drops per minute), alternating with milk and cream 600 ml. (50 drops per minute), for 7 to 10 days. Four patients were given 500 ml. intravenously thrice daily and by mouth received 3 oz. (85 ml.) milk and cream hourly. Phenobarbitone, "sodium amytal", and belladonna were also used as supplementary measures. Radiological evidence of ulcer disappeared in 9 cases. There has been no recurrence in these patients over the short period of 8 months. The buffering effect of amino-acids greatly reduces gastric acidity and the benefit is attributed to this. [In view of the rest in bed and supplementary feeding it is impossible to assess the value of this treatment.] *A. H. Douthwaite*

2112. **Peptic Ulcer in the Aged**
E. D. KIEFER and D. MCC. MCKELL. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **133**, 1055–1060, April 19, 1947. 4 refs.

This paper presents an analysis of 152 patients over 65 years of age in whom a diagnosis of peptic ulcer was made. Of these 77 had had their first symptom of ulcer after passing their sixtieth birthday. Only 69 patients gave a history considered characteristic of peptic ulcer, and the authors emphasize that this diagnosis must be considered in any elderly patient with a history of atypical digestive symptoms. Loss of weight was a prominent symptom, but uncomplicated cases responded as readily to ulcer treatment as did those in younger patients.

The authors emphasize the need for especially careful pre-operative preparation in cases of pyloric obstruction; haemorrhage offers the most serious threat to life. Surgical treatment should be undertaken in cases of haemorrhage before the patient has lost too much blood and become moribund, because the mortality rate in elderly patients with continued haemorrhage is very high; 31% of these patients had a history of haemorrhage, which in 4 instances was fatal. Follow-up of these patients showed 107 completely relieved, while 28 had recurrences, 4 were unimproved, and 8 had died; the length of time of observation is not given. Of 27 patients treated surgically by gastro-enterostomy or gastrectomy 2 died. The authors rightly indicate that the mortality rate in aged patients is directly related to the pre-operative preparation, the post-operative care, and the ability of the anaesthetist and the surgeon.

The differential diagnosis of ulcer and cancer is not discussed, but emphasis is laid upon the fact that a gastric ulcer in an elderly patient cannot be considered benign unless it disappears entirely under treatment and leaves no residual radiological sign, such as rigidity or fixation or mucosal defect. These findings should be confirmed by gastroscopy. *Thomas Hunt*

2113. **The Limitations of Roentgenology and Gastroscopy in the Diagnosis of Diseases of the Stomach: An Analysis of Fifty-three Proven Cases**
E. B. BENEDICT. *Gastroenterology* [*Gastroenterology*] **8**, 251–277, March, 1947. 10 figs., 3 refs.

The author assesses the relative value of radiology and gastroscopy in 53 cases of gastric lesions later verified at operation. This paper follows a previously reported series of 245 cases. Of 19 proven carcinomata, 10 were correctly diagnosed by both methods; in 1 case both methods gave incorrect results, and in the remainder gastroscopy was more accurate in 6 cases and radiology in 2. The other conditions discussed comprised: benign gastric ulcers (21 cases), jejunal ulcers (2), gastritis (5), benign tumours (2), lymphoma (1), and uncomplicated gastro-enterostomy stoma (1). Each case is discussed in detail, and the author concludes that if the gastroscopist can get a satisfactory view of the lesion he has more chance of arriving at a correct diagnosis than the radiologist. He stresses the fact that the greatest degree of accuracy is attained when both methods are used in co-operation. *N. S. Plummer*

2114. **Treatment of Gastric and Duodenal Ulcer with "Robuden".** (Die interne Behandlung des Ulcus ventriculi und Ulcus duodeni mit Robuden. Weitere Ergebnisse)
A. W. SURKES. *Schweizerische Medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **77**, 455–458, April 19, 1947. 18 refs.

In recent years American physiologists have isolated from the mucosa of the gastro-intestinal tract several hormone-like substances—for example, enterocrinin, which stimulates the production of sucus entericus, gastrin, a histamine-like substance, enterogastron, and urogastron, producing a marked diminution of the gastric secretion. The two last substances have already been used in ulcer therapy with benefit. Morrison (*Amer. J. digest. Dis.*, 1945, **10**, 323) has given the gastric juice of healthy persons to patients with gastric ulcer; in 8 of his 10 patients clinical symptoms disappeared within 2 days and the ulcer niche after 2 to 3 weeks. The present

author describes the results of treatment with a preparation made from stomach and intestinal extracts called "robuden", which had already been used in his hospital from 1942–5 on ulcer patients. Of 92 patients treated from January, 1944, to September, 1946, 28 (17 men, 11 women) had a gastric ulcer and 41 (36 men, 5 women) a duodenal ulcer. In all cases the diagnosis was verified radiologically. The patients were given twelve to twenty-one intragluteal injections of 1 ml. robuden and one robuden tablet by mouth three times daily; they still took the latter for 3 to 4 weeks after the end of the course of injections. The patients did not receive any other treatment, and after 4 to 6 days there was in general a distinct improvement. Those with severe symptoms were given 2 ml. robuden by injection and tolerated this dose very well. Of the 28 patients with gastric ulcer 18 were clinically cured—that is, they had no symptoms or physical signs of ulcer; 5 showed considerable improvement; and 5 derived no benefit. Of the 41 patients with duodenal ulcer 35 were clinically cured and 3 improved, while 3 had no result from the treatment. *X*-ray examination of 77 patients when they left hospital showed that of 26 with gastric ulcer 17 had been cured, no ulcer niche being present, while 5 showed that the niche was reduced in size; in 4 patients the niche was unchanged. Of 39 patients with duodenal ulcer 30 were cured, 6 improved, and 3 unchanged. Good results from robuden treatment have also been observed in cases of gastritis. The gastric acidity hardly changed, but in a few cases with previous hypoacidity normal acid values appeared.

The author summarizes the answers to a questionary sent to 76 patients 1 to 4 years after robuden treatment. Of these patients 28 had remained free from symptoms; 21 had had slight symptoms and 7 severe ones. In 5 *x*-ray examination had shown a recurrence, and 15 patients had been operated upon. The author recommends prophylactic treatment with robuden for ulcer patients by administration on the first 10 days of the months of one to two tablets three times daily.

[From the results obtained it hardly seems that robuden is a very efficacious remedy for gastric and duodenal ulcers.] *Paul Mayer*

2115. **Choice of Drugs in the Treatment of Duodenal Ulcer**

A. H. DOUTHWAITE. *British Medical Journal* [*Brit. med. J.*] **2**, 43–47, July 12, 1947. 8 figs., 18 refs.

The author believes, and presents evidence to show, that the action of belladonna in relieving the pain of duodenal ulcer is due not to any diminution of gastric acidity but to its power of diminishing excessive peristalsis and relieving spasm. He prefers to use *l*-hyoscyamine in doses of gr. $\frac{1}{120}$ (0·54 mg.) twice daily, since this is the component of atropine which has the most marked peripheral action. He considers the operation of vagotomy for duodenal ulcer to be unjustifiable, because the same result can be obtained by proper dosage of hyoscyamine.

The use of antacid drugs is criticized on the grounds that their action is transitory and variable, and that they may mask symptoms while the disease progresses. Continuous nasal drip-feeding with milk is the only effective method of continuously neutralizing gastric acidity. If this is impracticable, the author recommends 2-hourly feeds, with ½ oz. (14 ml.) of olive oil (to delay gastric emptying and to reduce acid output) and ½ oz. (15·5 g.) of magnesium trisilicate 2-hourly. Anxiety can usually be controlled by phenobarbitone gr. 1 (65 mg.) thrice daily, with a more potent soporific such as "sodium amytal" gr. 3 (0·2 g.) at night. Higher doses than this are not recommended. Instead, if phenobarbitone is unsatisfactory, the use of extractum cannabis indica (*B.P.C.*) gr. 4 (260 mg.) four times daily is suggested. The risk of addiction to this drug is said to be very slight if it is given in such dosage for limited periods of 1 or 2 weeks. The irritant quality of such substances as tobacco, mustard, vinegar, curry, alcohol, aspirin, and chloral hydrate is briefly discussed.

The author considers that drugs are required only during the period of active ulceration, and that once the ulcer has healed their continued use is unnecessary. Early symptoms of relapse are best treated with belladonna, and not with antacids. *John R. Forbes*

2116. **A Study of the Gastric Secretory Response in the Aged**

H. A. RAFSKY and M. WEINGARTEN. *Gastroenterology* [*Gastroenterology*] **8**, 348–352, March, 1947. 11 refs.

This study is based on a series of 47 normal persons who had no gastro-intestinal complaints beyond the usual degree of constipation found in old people. Three of the patients were between 65 and 69 years of age; 33 were between 70 and 79, and 11 between 80 and 85 years. Sixteen of the subjects were males and 31 were females. Fifteen-minute test-meal fractions were examined after the ingestion of two slices of toast and a glass of water. Those in whom no free hydrochloric acid was found were given 0·1 mg. histamine per 10 kilos of body weight. In all of the cases with achlorhydria the gastric contents were tested for ferments. After this test meal 53·2% of the whole group had 19 units or less of free hydrochloric acid; 17% were found to have true achlorhydria; and 12·7% hyperchlorhydria. No case of complete achylia gastrica was found.

The authors compare their results with other studies: they point out that the percentage with true achlorhydria is smaller than in other series, and stress the fact that hyperchlorhydria does occur in a few aged persons. The number of individuals tested in this study is relatively small, but the gastric analyses were more thorough than in most other series. *N. S. Plummer*

2117. **The Effect of Vagotomy on Gastric Function**

S. WOLF and W. DEW. ANDRUS. *Gastroenterology* [*Gastroenterology*] **8**, 429–434, April, 1947. 8 refs.

Bilateral supradiaphragmatic vagotomy was carried out on a man in the course of an operation for carcinoma of the oesophagus. A gastrostomy rendered repeated visual examination of the gastric mucosa feasible. No free hydrochloric acid was present before the operation.

Before vagotomy the mucosa was found to respond to emotional impulses in the same manner as in the now classical case of Tom. Thermal and painful sensations could be provoked. After vagotomy the sensibility of the stomach was unaffected; the mucosa usually became pale and no spontaneous motor activity was recorded. Mild hyperaemia and engorgement following a meal persisted. No emotional hyperaemia could be produced, however. Increase of motor activity and hyperaemia following prostigmin administration were still seen after vagotomy, but to a much smaller extent. The evidence clearly points to the assumption that the vagus nerves carry the efferent impulses concerned in the production of gastric hyperfunction, especially in relation to emotional impulses. *A. H. Douthwaite*

2118. **Giant Hypertrophic Gastritis**
S. N. MAIMON, J. P. BARTLETT, E. M. HUMPHREYS, and W. L. PALMER. *Gastroenterology* [*Gastroenterology*] **8**, 397–428, April, 1947. 26 figs., 24 refs.

The authors report on 6 cases of the comparatively rare condition of gross or giant hypertrophic gastritis. The difficulty of determining the diagnosis by radiology, gastroscopy, and test meal is equalled by the diversity and inconclusiveness of the symptoms. In fact, all 6 patients were subjected to operation because of the fear of malignancy. Papillomata formation is not unusual and is an indication for gastrectomy.

A. H. Douthwaite

2119. **Megaduodenum: An Attempt at Classification and Pathogenesis.** (A propos du mégaduodénum. Essai de classification et pathogénie)
P. HILLEMAND and M. DUGUÉ. *Archives des Maladies de l'Appareil Digestif* [*Arch. Mal. Appar. digest.*] **36**, 129–154, March–April, 1947. 23 figs., 34 refs.

The authors define the megaduodenum as a duodenum larger than normal, whatever the cause and whether the cause be apparent or not. They then classify the condition into: (1) congenital, (2) secondary, and (3) functional types.

Congenital varieties are rare, and may be caused by some other congenital lesion—such as narrowing or atresia of the distal segment or mesenteric compression associated with malrotation of the gut—or they may be of unknown aetiology. Secondary megaduodenum is caused by an acquired obstruction. Possible causes are: (1) compression by the superior mesenteric vessels (the authors consider that this is not common, and that it is too often wrongly diagnosed); (2) primary growth of the duodenum, jejunum, or neighbouring structures such as the pancreas; (3) secondary deposits in neighbouring lymph nodes; (4) tuberculosis of the jejunum or duodenum; (5) chronic pancreatitis; (6) periduodenal adhesions after cholecystitis. "Functional" megaduodenum is thought to be due to some disturbance of autonomic nervous function. Several cases, some with enlargement also of the colon or of other parts of the gut, are described in morphine addicts. The enlargement disappeared when the drug was discontinued. The authors discuss in some detail the possible mechanisms of production of the condition in such patients, and conclude that several factors are involved. Other cases of functional megaduodenum are said to be of endocrine origin; the condition has been observed in myxoedema and possibly in hypogonadism. It has also been seen in 2 cases of anorexia nervosa; here, too, the cause may be endocrine. Megaduodenum may also result from central disturbances; the case of an epileptic girl is cited, in whom excision of a cortical scar resulted in disappearance of the megaduodenum, and also, presumably, of the epilepsy; from "reflex" disturbances associated with duodenal ulcer (the authors claim to have found a megaduodenum in 18% of 520 cases of duodenal ulcer), gastric ulcer (20% of 298 cases of lesser-curvature ulcer), "chronic appendicitis", cholecystitis (10% of 15 (*sic*) cases), and other intestinal lesions. Finally, the authors admit that often they have been unable to find any cause for an apparently "functional" megaduodenum.

Treatment will naturally depend on the cause, but if no cause can be discovered duodeno-jejunostomy or splanchnic nerve block may relieve symptoms.

[This is an interesting paper on a subject little studied in Britain. The references given and observations cited are entirely from French sources. The authors do not in this paper state their criteria for considering a duodenum to be enlarged, though the radiographs of illustrative cases all show gross enlargement; nor do they tell us how commonly they diagnose the presence of megaduodenum. Few gastro-enterologists in Britain would agree with their high figures for its association with peptic ulcer. Some of the lesions given as "causes" for the so-called functional variety are probably merely coincidental conditions. Nevertheless, the authors have performed a service in drawing attention to some little known factors in the aetiology of an often puzzling condition, factors which the clinician would do well to bear in mind when faced with unexplained enlargement of the duodenum.]

John R. Forbes

2120. **The Formation of Concretions of Aluminum Salts of Fatty Acids after the Use of Aluminum Hydroxide**
G. P. CHILD, W. K. HALL, and S. H. AUERBACH. *American Journal of Digestive Diseases* [*Amer. J. digest. Dis.*] **14**, 63–64, Feb., 1947. 6 refs.

The authors describe a case in which small white concretions were found in the stools of a patient treated with aluminium hydroxide as an antacid after haemorrhage from a duodenal ulcer. The small masses, about 40 in number, were egg-shaped and varied from 5 to 25 mm. in length. They became more apparent after the melaena had cleared up, and their passage was accompanied by intermittent periods of constipation and diarrhoea, cramps, and pain suggestive of gastro-intestinal irritation. The patient had experienced a similar sequence of events after a haemorrhage 4 years previously. Chemical tests indicated that the concretions consisted of aluminium salts of fatty acids together with a small amount of neutral fat. The site of origin of the soaps was open to speculation, the size and convoluted markings pointing to compression in some hollow

viscus of small calibre. The condition cleared up after 5 days, apparently with an increase in the diet. The authors were unable to discover any previously recorded description of such concretions after the use of aluminium hydroxide, but they cite a case of complete intestinal obstruction after it had been given in the treatment of severe haemorrhagic ulcer. At necropsy a large mass consisting of blood clot and aluminium hydroxide was found to be obstructing the bowels.

[This case is evidently most unusual but may serve as a caution against the indiscriminate use of aluminium hydroxide as an antacid. The doses employed are not mentioned, but it is known that aluminium chloride is formed in the stomach from the hydroxide and may irritate the intestine. Moreover the drug has no power to prevent the formation of the Mann-Williamson ulcer in dogs, and it would seem wise to limit its use to the active stage of ulcer treatment only and to avoid it in prophylaxis, and perhaps also in cases of haemorrhage until the bowels are moving freely. The matter is well discussed by Bockus (*Gastro-enterology*, Vol. 1, Philadelphia, 1943).] *T. L. Hardy*

INTESTINES

2121. **Plasma and Corpuscular Cholesterol in Sprue**
J. S. Robson. *British Journal of Experimental Pathology* [*Brit. J. exp. Path.*] **28**, 152–160, April, 1947. 32 refs.

It is possible that defective fat absorption in sprue may be due to causes other than defective phosphorylation. Cholesterol is a likely carrier of fatty acids across the intestinal wall. The author therefore estimated the plasma and corpuscular cholesterol, both free and combined, in 5 patients with sprue and in 5 normal controls. The estimations were first made on the blood of fasting subjects, and then at intervals during the absorption of 18 g. of milk fat. The differences between the various mean values in patients and controls were subjected to the "t" test for significance.

The mean level of the fasting total plasma cholesterol in sprue (146 mg. per 100 ml.) was significantly lower than in the controls (206 mg. per 100 ml.). The fasting plasma cholesterol ester in sprue (mean 2·81 milliequivalents per litre) was significantly lower than in the controls (mean 3·92 milliequivalents per litre). Both groups had a normal ratio of esterified to total fasting plasma cholesterol, and there was no significant difference between their mean fasting corpuscular cholesterol levels.

During the absorption of the fat meal the total plasma cholesterol increased in the controls (mean increase 10·5 mg. per 100 ml.), but decreased in the patients (mean decrease 8·35 mg. per 100 ml.); the difference was statistically significant. In both groups the plasma cholesterol ester rose to a similar extent. It followed that in sprue there was a fall in the free plasma cholesterol (mean fall 15·4 mg. per 100 ml.), contrasted with a rise in the controls (mean rise 3·84 mg. per 100 ml.). The difference was statistically highly significant. In both groups the total corpuscular cholesterol showed inconstant changes, but cholesterol ester appeared in the red cells of all the controls and of only 1 of the patients. It was not found in the red cells of any fasting subject.

The author concludes that: "the abnormal changes in blood cholesterol during fat absorption in a disease in which fatty acid absorption is known to be defective is presumptive evidence that the two phenomena are closely related." He suggests that there may be a diminished formation or absorption of cholesterol esters in the intestine.

[This paper is marred by careless proof-reading. For example, "mg. per ml." appears five times in the text instead of mg. per 100 ml.] *Martin Hynes*

2122. **Syndromes of Non-tropical Sprue with Hitherto Undescribed Lesions of the Intestine**
J. Schein. *Gastroenterology* [*Gastroenterology*] **8**, 438–460, April, 1947. 4 figs., 90 refs.

The various theories concerning primary atrophy, atrophy secondary to inflammation, and inflammation with ulceration of the small gut in relation to sprue are reviewed.

The author reports details of a 15-year-old boy alleged to have non-tropical sprue. [Since his red cell count was 5,000,000 per c.mm. and the superficial and intra-abdominal lymph nodes were enlarged, the accuracy of the diagnosis is open to doubt. Among the vast number of investigations done, there is no record of details of fat absorption and the fatty composition of the stools. It will be clear, therefore, that the report on clubbing of the villi with hyaline material is of doubtful significance.] *A. H. Douthwaite*

2123. **Treatment of Tropical Sprue with Folic Acid**
R. J. G. Morrison and C. R. St. Johnston. *Lancet* [*Lancet*] **1**, 636–637, May 10, 1947. 8 refs.

The progress of 4 cases of tropical sprue treated with synthetic folic acid is described. Two cases, previously untreated, showed a dramatic improvement both in the blood and in intestinal absorption. The other 2 cases, which were of long standing and had long been treated with liver, were improved subjectively, but little or no effect on the blood was observed.—[Authors' summary.]

LIVER; GALL-BLADDER

2124. **Chronic Subclinical Impairment of the Liver. Early Diagnosis and Treatment. Further Improvement and Evaluation of Certain Liver Function Tests**
J. G. Mateer, J. I. Baltz, H. H. Steele, S. W. Brouwer, and J. R. Colvert. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **133**, 909–916, March 29, 1947. 27 refs.

Continuing their work on tests of liver function these authors describe eleven different tests and give what they consider normal values for them. The tests vary in sensitivity, and it is claimed that by using the three most delicate ones (cephalin flocculation, thymol turbidity at *p*H 7·55, and a new bromsulphalein test) cases of subclinical liver damage can be detected. Clinical details

of these patients are not given and apparently biopsies of the liver were not done, so that it is uncertain whether these were merely examples of damaged liver function or whether actual structural changes were present. In addition to their description of the tests the authors indicate different combinations of these which they advise in the various types of liver disease.

The detection of sub-clinical liver damage is regarded as important, for these workers maintain that the treatment of such cases with a high-carbohydrate, high-protein, low-fat diet (C 350 to 400 g.; P 125 to 150 g.; F 35 g.) with added vitamins (A and B complex) causes the sensitive tests to return to normal and prevents the development of permanent damage or cirrhosis. It is not stated whether the patients are ambulant or whether strict rest in bed is enforced. *Christopher Hardwick*

2125. **Pancreatic Secretion in Hepato-biliary Diseases.** (La sécrétion pancréatique au cours de certaines affections hépato-biliaires)
K. HERFORT. *Gastroenterologia* [*Gastroenterologia, Basel*] **72**, 51–59, 1947. 4 refs.

Chronic pancreatitis is usually secondary to gall-stones or cholecystitis. Surgeons first noticed at operations performed for acute pancreatitis that the bile ducts were always involved, while at gall-bladder operations they often found increase in size of the head of the pancreas.

The author studied the pancreatic secretion in cases of liver damage caused by cirrhosis, infective hepatitis, and acute atrophy of the liver. He had previously examined the external secretion of the pancreas in 60 cases of "cholecystopathy". In 36 of the cases involvement of the pancreas manifested itself clinically and in laboratory tests. In one-quarter of his cases he could not prove involvement of the pancreas. The participation of the pancreas in liver affections has not been studied much.

In Eppinger's opinion (*Die Leberkrankheiten*, Berlin, 1937) there are 4 groups of cirrhosis: (1) with predominant lesions in the liver; (2) with lesions in the liver and spleen; (3) with involvement of the peritoneum in addition to the liver and spleen; (4) with pancreatic lesions added to the previous ones. The present author examined 20 patients with cirrhosis, 12 males and 8 females. Pancreatic external secretion was assessed by analysis of the faeces and enzyme estimation of the duodenal juice after stimulation of the secretion by intravenous injection of secretin or intramuscular or oral administration of vitamin A. The results showed that lipase is the enzyme whose secretion is first diminished, much before that of trypsin. Lack of lipase could be shown by examination of the faeces in 3 cases only. It is well known that the splitting of fats can occur through action of intestinal bacteria to such a degree that no deficiency of pancreatic lipase in the faeces can be detected, although disturbance of the pancreatic secretion can be proved. Lipase estimations by the method of Bondi modified by Chiray proved accurate. In 9 out of 20 cirrhotic patients pancreatic secretion was seriously disturbed. The deficiency of lipase was most marked, in contrast with the even decrease in pancreatic enzymes in cases of tumour. The degree of the pancreatic insufficiency is not parallel with the severity of the cirrhosis.

Twenty-three cases of infective hepatitis were examined; 8 showed a disturbed pancreatic function. The amount of pancreatic juice obtainable 15 to 20 minutes after secretin injection was not more than 2 to 4 ml., while the normal response is 80 to 120 ml. Pancreatic secretion increased during convalescence but remained below normal (under 20 to 40 ml.). Tryptic activity was more quickly restored than lipolytic. Of the 8 cases showing decrease in pancreatic function 4 had a considerable insufficiency after the disappearance of the jaundice. Two cases of acute yellow atrophy of the liver after cincophen administration were examined. The secretion of duodenal juice was normal after secretin injection. Both patients died and the histology of the pancreas did not show any abnormality. *E. Forrai*

2126. **Liver Dysfunction in Rheumatic Heart Disease. Preliminary Report**
R. W. KISSANE, R. S. FIDLER, and T. E. CLARK. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **213**, 410–412, April, 1947. 6 refs.

In an attempt to determine whether liver dysfunction occurs only at the time of heart failure or whether it is a gradually developing process in rheumatic carditis, 137 cases were submitted to the cephalin–cholesterol flocculation test. A positive result was obtained in 72%. The test was positive in 89% of patients with cardiac failure, in 82% of those with auricular fibrillation, in all of those with interventricular block, and in 69% of those with first and second degree cardiac function. There was no connexion between the degree of the positive cephalin–cholesterol flocculation reaction and the degree of functional severity of the rheumatic heart disease.
Geoffrey McComas

2127. **Toxicity Studies of α (4-Hydroxy-3,5-Diiodo-Benzyl-*N*-Butyric Acid) and α (4-Hydroxy-3,5-Diiodo-Benzyl-*N*-Caproic Acid): Compounds Proposed as Gall Bladder Contrast Agents**
D. M. GRAYZEL and S. NATELSON. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **32**, 292–295, March, 1947. 1 ref.

A 25% solution of α-4-hydroxy-3,5-diiodo-benzyl-*n*-butyric or -*n*-caproic acid was given intravenously to cats. The first was lethal at 500 mg. per kilo body weight and the second at 375 mg. per kilo. Petechial haemorrhages were present in the lungs and cloudy swelling in the liver and kidneys. Both substances given by mouth in doses up to 1 g. per kilo caused only transient loss of appetite.
V. J. Woolley

2128. **The Influence of an Antacid (Non-reactive Aluminium Hydroxide Gel) on the Evacuation of the Bowels and the Fecal Column. (Introducing a Standardized Method for the Clinical Study of Constipating Effects of Drugs)**
A. X. ROSSIEN and A. W. VISTOR. *American Journal of Digestive Diseases* [*Amer. J. digest. Dis.*] **14**, 226–229, July, 1947. 8 refs.

Endocrine Disorders

THYROID GLAND

2129. **The Effect of Goitrogenic and Other Reducing Agents on Inactivated Thyrotropic Hormone Extract**
A. ALBERT, R. W. RAWSON, P. MERRILL, B. LENNON, and C. B. RIDDELL. *Endocrinology* [*Endocrinology*] **40**, 299–302, May, 1947. 1 ref.

The study of the effect of reducing agents on iodine-inactivated thyroid-stimulating hormone has been continued. It was found that a number of reducing substances, some of which were goitrogenic and some non-goitrogenic, restored the thyrotrophic activity. This effect is considered to be a direct action, since the substances themselves when used in the same dosage were without thyrotrophic effect. *E. F. Scowen*

2130. **Augmentation of Thyrotropic Potency by Goitrogens**
A. ALBERT, R. W. RAWSON, P. MERRILL, B. LENNON, and C. B. RIDDELL. *Endocrinology* [*Endocrinology*] **40**, 303–307, May, 1947. 3 refs.

Additional data are given to show that the exposure of pituitary thyrotrophic extracts to various goitrogenic compounds results in an increase of thyrotrophic activity, even when the goitrogenic substance is presumably removed before assay. *E. F. Scowen*

2131. **Muscular Dystrophy in Hypothyroidism.** (Les dystrophies musculaires des hypothyroïdiens)
L. RIMBAUD and P. PASSOUANT. *Revue Neurologique* [*Rev. Neurol.*] **79**, 81–96, Feb., 1947. 5 figs., 20 refs.

In myxoedema, muscular hypertrophy or atrophy may occur, with or without myotonia. These abnormalities appear in a muscle which is apparently quite healthy.

Hypertrophy in acquired hypothyroidism is generalized, though sometimes individual muscle groups only are affected—for instance, the thenar muscles. They feel firm when palpated, are rigid when moved passively, and are painful. The first case the authors describe was that of a man, aged 45, who came into hospital in November, 1943, for gastrectomy; he was treated for syphilis and discharged, but returned in September, 1944, with oedema of the lower limbs, myxoedema (basal metabolism −22%), and hypertrophy chiefly of the scapular and pelvic muscles; this spread to other groups, but biopsy showed the muscle fibres to be quite normal. The patient died in May, 1945, from an intercurrent pulmonary infection, but no abnormality of the muscles could be found post mortem. In congenital myxoedema the above findings are usual, but the reaction of degeneration is usually absent. Treatment with thyroid extract not only acts on the myxoedema, but to a certain extent relieves the muscular hypertrophy in some cases. The second case was that of a 10-year-old boy whose gait was never normal, but waddling and ataxic. When he was aged 7 it was first noticed that his muscles, mainly those of arms and shoulders, were not developing normally, and glycine was given, 15 g. daily. Three years later he entered hospital with myxoedema; all his muscles were firm but weak, those of the pelvis and lower limbs being hypertrophied; reaction of degeneration was absent. Thyroid extract was given, from 0·1 to 0·8 g. daily, and there was slight improvement in the mental state but no muscular change. Commenting on these cases, the authors suggest that age merits consideration; in some cases the muscle change starts soon after birth, in others at puberty, and in some at about the " menopause " in both sexes. This is significant in the light of the parallel development of hypothyroidism and muscular dystrophy. Few cases can be studied pathologically, for biopsies are rare and necropsies rarer still. The muscle fibres vary in size, some being much enlarged and others atrophied. There is a decrease in transverse striation, which sometimes reappears after thyroid treatment; side by side with normal fibres are found others filled with polymorphonuclear leucocytes and lymphocytes, not characteristic of an inflammation. Only a difference of degree separates the changes in hypothyroidism from the congenital myopathies. Lympho-histiocytes are found infiltrating the thyroid lobules, which themselves are proliferating. Sclerosis is seen in the anterior pituitary gland, and atrophy in the suprarenals. Nothing abnormal is observed in the central nervous system.

The cause may lie in the thyroid deficiency, but the authors believe that the primary cause is an action of the diencephalon. They carried out researches with the idea that prolonged action of acetylcholine at the myoneural junction might be found, but not only was acetylcholine not identified, but cholinesterase was elevated. Other points considered were the sympathetic innervation of voluntary muscle (possibly indirectly through the liberation of adrenaline), and disturbances in muscular metabolism, particularly of proteins and lipids, potassium and calcium. Although this study of myopathies in hypothyroidism does not throw much light on the ultimate causes, it may point the way to finding effective treatment in certain cases. *T. E. C. Early*

2132. **Mechanism of the Therapeutic Effect of Iodine in Hyperthyroidism.** (Mecanismo de la acción terapéutica del yodo en el hipertiroidismo)
E. DE ROBERTIS. *Medicina* [*Medicina, B. Aires*] **7**, 157–167, April, 1947. 5 figs., 24 refs.

The author traces the history of the use of iodine in the treatment of goitre and refers to the various explanations brought forward to explain its action on the gland. Three theories are discussed: (1) The mechanical one of Marine (1927), who states that iodine interferes with the passage of colloid into the circulation. This is

amplified by Mosser, in whose view the accumulated colloid compresses the secretory epithelium and hence reduces its activity. (2) That of " mass action " introduced by Salter and Lerman (1936), who consider that the synthesis and breakdown of thyroid protein is of enzymatic nature. In thyrotoxicosis breakdown is excessive and iodine would act as a catalyst in the direction of synthesis. (3) The theory that there is a proteolytic enzyme in colloid; this is supported by the author. He arrived at this conclusion by analysing the proteose content of colloid material extracted by microdissection of the thyroid follicles of rats. The extracted colloid, after having been buffered, was observed under the microscope to digest a thin film of gelatin. If the enzyme was present in high concentration, there would be extensive digestion of the gelatin. The enzyme was in highest concentration in the hyperactive thyroid. It acts by splitting thyroglobulin, which has a very high molecular weight, into simpler compounds, which then pass into the circulation. According to the author the intensity of the proteolytic process in rats given potassium iodide varies according to the length of treatment; it is high in the first 5 to 12 days and reduced after 45 days.

The author claims that these findings are analogous to those in the human subject. He measures photometrically the proteolytic enzyme of the human thyroid by its action in digesting edestin. Administration of iodine inhibits the action of the enzyme and so colloid accumulates in the follicle. Experiments were also carried out *in vitro* on glycerin extracts of toxic thyroid; when iodine was added there was a reduction in proteolytic activity as measured by the breakdown of edestin. The iodine must be in molecular form and not ionic in order to inhibit the toxic activity of the gland. Another conclusion from the experiment was that thiourea does not affect proteolytic activity; it must act in some other way. The author thinks that iodine may also tend to prevent the synthesis of thyroxine. *Paul B. Woolley*

2133. **Antithyroid Activity of Ergothioneine**
A. LAWSON and C. RIMINGTON. *Lancet* [*Lancet*] **1**, 586–587, May 3, 1947. 1 fig., 14 refs.

Ergothioneine, the methyl betain of 2-thiol-histidine, was isolated from Hungarian ergot of rye by a modification of the Pirie procedure and purified by mercuric chloride precipitation, giving a yield of 0·1% ergothioneine. The antithyroid activity was assayed by determining the iodine content of thyroid glands by colorimetric measurement of the starch-iodine reaction described by Talbot, which allows accurate determinations of 1 to 20 μg. iodine. The activity of ergothioneine was compared with that of thiouracil by administration of daily subcutaneous injections of one or the other for 10 days to groups of 5 rats in doses of 0·2, 0·5, 0·75, and 2 mg. per kilo body weight. The antithyroid activity of the two substances is of the same order, although there is greater variability in the case of ergothioneine. The authors suggest that the greater variability may be due to differences in the amount of ergothioneine present in the blood before the experiment was started. The variation in man had been reported to be from 3 to 10 mg. per 100 ml. blood corpuscles. As ergothioneine is present in the blood in quantities which exert a definite antithyroid activity, investigation of the possible occurrence of significant variations in persons with disturbance of thyroid function is in progress. It is suggested that the naturally occurring ergothioneine may produce less toxic symptoms when used as a therapeutic agent than do synthetic compounds. *S. A. Simpson*

2134. **Effect of Aminothiazole on the Adrenal.** (Action de l'amino-thiazol sur la surrénale)
J. P. LAVEDAN. *Comptes Rendus des Séances de la Société de Biologie* [*C.R. Soc. Biol., Paris*] **141**, 338–339, April 26, 1947. 4 refs.

The results of experiments on the relations which exist between thyroid and adrenal still present many contradictions. Aminothiazole ("abadol") was injected into prepuberal and adult rats of both sexes (0·25 g. per kilo daily for a month). The weight of their adrenals did not differ from that of controls, but the structure of the fasciculate and reticular zones was greatly altered in the treated rats. The fasciculate zone loses striation and the cell columns are cut up. Numerous vacuoles are found. The intracellular lipids are at first broken up into particles, which coalesce and form great masses flattening the nuclei against the cell walls. Confluence of these gives rise to an appearance like that of gruyère cheese. The reticular zone is packed with vacuoles. The condition implies great fat reserves. It is the antithyroid action of aminothiazole which leads to these results. They are not revealed by thyroidectomy. In contrast to the effects of thiouracil, the adrenal medulla is scarcely affected.
D. T. Barry

2135. **Effect of Aminothiazole on the Pituitary Gland.** (Action de l'aminothiazol sur l'hypophyse)
J. P. LAVEDAN. *Comptes Rendus des Séances de la Société de Biologie* [*C.R. Soc. Biol., Paris*] **141**, 339–340, April 26, 1947. 6 refs.

The anterior lobe of the hypophysis of rats treated with aminothiazole shows a great diminution of eosinophil cells which are converted to chromophobe elements. The basophil cells still exist but in distinctly reduced numbers. *D. T. Barry*

2136. **Effect of Iodine and Adrenalin on Thyrotropin in Graves' Disease and in Normal and Thyroidectomized Dogs**
L. J. SOFFER, M. VOLTERRA, J. L. GABRILOVE, A. POLLACK, and M. JACOBS. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **64**, 446–447, April, 1947. 4 refs.

By biological assay the amount of circulating thyrotrophic factor was estimated in clinical hyperthyroidism, the effect of iodine on the circulating thyrotrophic factor was determined, and the influence of parenteral injections of adrenaline on the thyrotrophic discharge from the anterior pituitary in the intact and in the thyroidectomized animal was measured.

In the first study young guinea-pigs were given 5 ml. of serum from the patient or an experimental animal on 2 successive days and killed with ether 24 hours later. Their thyroid lobes were then fixed in 10% formalin, stained with haematoxylin–eosin, and examined; there was decrease in colloid, increase in cells lining the acini, and sometimes mitosis, changes like those seen in patients with Graves's disease.

For the second experiment specimens of blood obtained from patients with Graves's disease before treatment and on the second, fourth, sixth, eighth, and eleventh days after iodine treatment had been started were injected as above into guinea-pigs; thyroids were removed 24 hours later and examined. For the third experiment normal dogs were used, 1 ml. of adrenaline in oil being injected twice daily; one lobe of the thyroid was removed on the fourth day, and the second 10 days later. Another group of animals was similarly treated, but total thyroidectomy was performed first, and blood specimens were taken 2, 4, 6, 8, and 10 days after.

In all of the 13 patients with Graves's disease studied thus, there was less circulating thyrotrophic factor than is present in normal individuals. The amount increased when iodine was given, rose to a peak between the fourth and sixth days, and then began to fall; a further slight increase occurred after subtotal thyroidectomy in patients with Graves's disease. In 3 cases the hyperplastic changes in the guinea-pig thyroids were profound; in the remaining 10 they varied from slight to moderate. In controls treated with iodine there was a barely perceptible increase.

After injection of adrenaline in oil marked hyperplastic changes appeared in the lobe removed on the fourth day; the other lobe, removed on the fourteenth day of injection, showed considerable decrease in hyperplasia. In totally thyroidectomized dogs the adrenaline caused marked increase in thyrotrophic factor until about the fourth to sixth days, when a decrease began.

T. E. C. Early

SUPRARENALS

2137. **A Study of the Metabolism in Addison's Disease. I. On Carbohydrate and Phosphorus Metabolism.** [In English]
O. HELVE. *Acta Medica Scandinavica* [*Acta med. scand.*] **127**, 543–564, May 17, 1947. 73 refs.

Earlier studies of the carbohydrate and phosphorus metabolism in Addison's disease are reviewed.

The present investigations were carried out in 32 cases of Addison's disease, and a comparison with values in 40 normal people was undertaken. The fasting blood sugar in all of the 32 cases showed no significant deviation from the normal, and treatment with desoxycorticosterone acetate and a low potassium diet or by high sodium-chloride intake was without obvious effect on the blood sugar. A glucose-tolerance test was performed on 23 cases; its results in all were within normal limits, and in 10 cases the adrenaline-tolerance test showed little if any deviation from the normal.

An investigation of the total blood phosphorus and of its component fractions revealed a slight rise in inorganic phosphate, in spite of a suggestion of a fall in the total phosphorus in 6 patients. Treatment with desoxycorticosterone acetate did not affect this, and the blood-phosphorus changes in response to the administration of glucose, adrenaline, and insulin were essentially the same as in the controls.

E. F. Scowen

2138. **The Constitutional Type of Precocious Puberty**
A. M. HAIN. *Journal of Clinical Endocrinology* [*J. clin. Endocrinol.*] **7**, 171–185, March, 1947. 2 figs., 36 refs.

The causes of precocious puberty are reviewed, and a series of 7 patients, 5 girls and 2 boys, with this condition is described. All these cases showed an increase of gonadotrophin in the urine equivalent to an adult excretion, and in all there was some increase in the 17-ketosteroid output for their age group. The highest figure was 6 mg. in 24 hours at the age of 6½ years. In 2 cases a pregnane derivative was excreted in the urine which is at present unidentified. The mechanism of the production of these manifestations is discussed.

E. F. Scowen

2139. **Factors Concerned in the Circulatory Failure of Adrenal Insufficiency**
A. P. W. CLARKE, R. A. CLEGHORN, J. K. W. FERGUSON, and J. L. A. FOWLER. *Journal of Clinical Investigation* [*J. clin. Invest.*] **26**, 359–363, May, 1947. 31 refs.

SEX GLANDS

2140. **Studies on Hypometabolism. II. Hypogonadism. A Nosological Unit in Young Women.** [In English]
E. D. BARTELS and P. HJORTH. *Acta Medica Scandinavica* [*Acta med. scand.*] **127**, 313–341, April 25, 1947. 2 figs., 15 refs.

During the German occupation of Norway a common finding among the population was loss of weight, but many doctors were impressed by the large number of young women who complained of obesity and menstrual disturbance. It was noted that many had a low basal metabolic rate (B.M.R.) [a finding rare in obese patients in England and America]. The authors take the view that the condition was not, in fact, provoked by war conditions, but had hitherto been hidden under the various diagnoses made by the specialists to whom the patients presented themselves, the choice of specialist and therefore the choice of diagnosis depending on the main symptoms. Thus, in their view, cases have previously been labelled secondary amenorrhoea, adiposity, myxoedema, mental depression, cardiac neurosis, hypothalamic disorder, and " nuchal myosis ".

Fifty cases are described. The story of each patient is approximately the same. A hitherto healthy young woman with normal menstruation begins to put on weight. At the same time the menses become scanty or cease, libido decreases, and various nervous symptoms are noted. The authors' conclusions from their investigations are as follows. (1) That in a high proportion of

their patients there was depression of ovarian function [the conclusion appears likely on clinical grounds, but the laboratory investigations, on which much stress is laid, are of no significance]. (2) That the B.M.R. is lowered. [The figures given do not suggest that a lowered B.M.R. is an important part of the syndrome. The authors themselves stress, correctly, the absence of any correlation between adiposity and hypometabolism.] (3) That changes in hair growth are common—dryness, greasiness, falling of the hair, and splitting of the hair being present in over half the cases; these changes were not obvious on clinical examinations. (4) That nervous complaints occurred in almost every case, the commonest being tiredness, anxiety, and depression often associated with such autonomic signs and symptoms as acrocyanosis, hot flushes, and undue perspiration. The authors draw attention to the possibility that there is a central nervous origin of these symptoms and indeed of the whole syndrome.

[Many of the signs and symptoms of this " syndrome " are inconstant, and a few of the cases described seem to be " dragged in " with some difficulty, but it would appear that two features are almost constant—increase in weight and depression or anxiety. The authors are not apparently aware of previous work on this association. The abstracter drew attention to it in 1946 (*Postgrad. med. J.*, **22**, 169), and explained it on the basis of Verney's work on the relation between emotion and water retention. Verney and his associates (for references see the above paper) showed that in dogs, anxiety, probably by way of the hypothalamus, caused an increase in posterior pituitary secretion, with a consequent diminution of water excretion. Greene suggested that the " adiposity " which he had observed as a system of anxiety was due largely to water retention and was of similar causation. A re-examination of their patients by Bartels and Hjorth would probably suggest that " hypogonadism " is a title which stresses unduly a relatively unimportant and inconstant feature of the syndrome. They might also be inclined to revise their view that the occupation of Norway by the Germans had no influence on its incidence.] *Raymond Greene*

2141. **Studies on the Functions of the Hypophyseal-diencephalic System and of the Ovaries by means of Radioactive Phosphorus.** [In English]
U. Borell, A. Westman, and A. Örström. *Gynaecologia* [*Gynaecologia, Basel*] **123**, 186–200, March, 1947. 2 figs., 14 refs.

These studies are based on the results of experiments upon anoestral and oestral female rabbits injected at predetermined intervals before and after coitus and upon castrates 3 to 5 weeks after oöphorectomy. Each animal received approximately 0·1 millicurie of radioactive phosphorus, P^{32}, as free phosphate in 1 ml. 5% glucose solution intravenously. Animals were killed by decapitation 30 minutes after the injection of radioactive phosphorus. Analyses were carried out on blood, cerebellum, tuber cinereum, anterior lobe of the pituitary, and ovaries. Total radioactivity was expressed in impulses per minute and total phosphate in μg. Hevesy (*Ann. Rev. Biochem.*, 1940, **9**, 641) showed that radioactive phosphorus behaves metabolically in the same way as phosphorus. Thus, the metabolic activity is proportional to the percentage of radioactive phosphorus. The cerebellum was chosen as a standard, and the relative specific activity in the other organs was determined. The experimental results, with statistical analysis, are set out in four tables and two figures. The experiments show the striking influence of coitus upon the tuber cinereum and the anterior lobe of the pituitary, while the effect upon the ovaries is delayed and reaches a second peak at ovulation. The method provides obvious advantages over the previously employed procedures of section and extirpation. *Magnus Haines*

2142. **Variations in Blood Calcium due to Androgens and Oestrogens.** (Les variations de la calcémie par les androgènes et les œstrogènes)
H. P. Klotz and P. Barbier. *Annales d'Endocrinologie* [*Ann. Endocrinol.*] **8**, 57–61, 1947. 21 refs.

The present position of the authors' researches into the effect of a single injection of androgen or oestrogen on the blood calcium in human subjects is briefly described. A single injection of an ester of testosterone (20 mg.) produces in both sexes a rise in blood calcium, beginning within 2 hours and occurring even in parathyroidectomized subjects. Phosphate excretion in the urine was not increased nor was the mineral phosphate content of the blood lowered. This action of testosterone is in every way comparable to that of its chemical analogue, calciferol.

The authors also recapitulate their work, previously reported, on the effect of a single dose of 20 mg. oestradiol benzoate. This produced a lowering of blood calcium in the subjects of latent tetany of both sexes, and particularly in parathyroidectomized subjects, but was without effect in this respect on normal persons.

S. S. B. Gilder

2143. **The Effect of the Prostate and Seminal Vesicle on the Production of Hyaluronidase by Rat Testes Homogenate**
S. L. Leonard, P. L. Perlman, and R. Kurzrok. *Endocrinology* [*Endocrinology*] **40**, 199–201, March, 1947. 6 refs.

Hyaluronidase is an enzyme formed by mammalian sperm which will disperse the follicle cells surrounding the newly shed ova of mammals; it may play a part in preparing the eggs for sperm penetration. The authors found that the concentration of this enzyme was higher in the uterine fluid of rats after mating than in testis extracts, suggesting either that the method of extraction was faulty or that the other constituents of the seminal fluid favoured the production of the enzyme.

Experiments showed that both suppositions were correct. First, if the testes were incubated for 8 hours at 37° C. the yield of hyaluronidase in the homogenate was increased about 100% above that found in homogenates maintained at 10° C. Secondly, the yield of enzyme was doubled again if the incubation was carried

out in the presence of homogenized seminal vesicle tissue. Prostate tissue had little or no effect. Some hyaluronidase was found both in seminal vesicles and in prostate glands, but the concentration was low (lower in the first than in the second); probably hyaluronidase passes by diffusion from the sperm in the ductus deferens.

It is recalled that Mann (*Biochem. J.*, 1946, **40**, 481) has shown that fructose is the prime energy source for sperm, and that it occurs in highest concentration in seminal vesicles or prostate gland according to species.

Peter C. Williams

PITUITARY

2144. **The Essential Lesion in Experimental Diabetes Insipidus**

P. HEINBECKER, H. L. WHITE, and D. ROLF. *Endocrinology* [*Endocrinology*] **40**, 104–113, Feb., 1947. 6 figs., 8 refs.

The authors, writing from the Washington University School of Medicine, St. Louis, suggest that the term "hypophysectomy" is meaningless unless defined and qualified. They distinguish between total hypophysectomy (operations in which all divisions of the hypophysis, including median eminence and stalk, are removed or rendered functionless) and simple hypophysectomy (operations short of total hypophysectomy but including total removal of the pars distalis).

Total hypophysectomy in 15 dogs was followed by marked sustained diabetes insipidus with eightfold to twentyfold increases in urinary output; 5 totally hypophysectomized dogs in which this polyuria was not sustained suffered from infection with abscesses in the hypothalamus or distension of the third ventricle and loss of appetite and weight. The only difference between the totally hypophysectomized dogs and those with diabetes insipidus produced by denervation of the neurohypophysis is that the former show a very slow decrease in their urinary output; so slow, indeed, that even 30 months after operation the output is still several times greater than normal. When the pars distalis was removed from the animals with denervated neurohypophyses there was a slight temporary increase in polyuria followed after several weeks by a slow decline. The urinary output of two totally hypophysectomized dogs (in three experiments) was increased by daily injections of 6 mg. of desoxycorticosterone acetate, doubled when this treatment was augmented by daily doses of dried thyroid (0·1 g. per kilo orally), but again reduced when anterior pituitary extract was given as well, thus demonstrating an antidiuretic action of the anterior pituitary.

From these results the following conclusions are drawn. The presence of the pars distalis *per se* is not essential for the development of diabetes insipidus: the slow fall in the degree of polyuria after total hypophysectomy is due to slow atrophy of the adrenal cortex and thyroid glands. On the other hand, the presence of the pars distalis may prevent the appearance of diabetes insipidus where removal of the neurohypophysis is incomplete (as when it is denervated by puncture or section of the stalk); in this case the development of polyuria depends on the amount of functional neurohypophysis remaining—enough may be removed to initiate polyuria but yet leave some functional tissue; it is suggested that the removal of this remnant accounts for the stimulus to polyuria when the pars distalis is removed.

[This field of research is a controversial one, probably because of species differences and the difficulty of demonstrating the exact limits of operative interference. Although no mechanism is suggested for the actions propounded in the last sentence of the preceding paragraph, the hypothesis fits the results of the experiments and the conclusions appear reasonable and suggestive.]

Peter C. Williams

2145. **Regulation of Pituitary Adrenocorticotrophic Activity During the Response of the Rat to Acute Stress**

G. SAYERS and M. A. SAYERS. *Endocrinology* [*Endocrinology*] **40**, 265–273, April, 1947. 1 fig., 13 refs.

The activity of pituitary adrenocorticotrophin in the rat is assessed by measurement of the ascorbic-acid content of the adrenal glands. It is shown that this is reduced within an hour by exposure to cold (4° C.), or heat (38° C.) or by the injection of adrenaline (4 μg. per 100 g.), histamine (0·5 mg. per 100 g.), or killed typhoid organisms. The reduction in all these cases is much the same—from about 420 to about 310 mg. per 100 g. fresh tissue. The reduction can in every case be prevented by the injection of adrenal-cortical extract. A similar reduction is brought about by the injection of adrenocorticotrophin, and this reduction is not prevented by the injection of cortical extracts. It is concluded that stress leads to an increased adrenocorticotrophin output from the pituitary, which is induced by a fall in concentration of adrenal steroids.

The reduction in adrenal ascorbic acid is graded according to the degree of cold to which the adult male rats are exposed or to the dose of histamine injected. The degree to which the reduction may be abolished is related to the dose of cortical extract injected. Thus, different types of stress may be qualitatively evaluated in their effects and different adrenal steroids assayed for their potency in withstanding these conditions. Preliminary assays of several cortical steroids in preventing the enhanced output of adrenocorticotrophin caused by cold and histamine stresses give their relative activities as 17-hydroxycorticosterone=4, corticosterone=1, desoxycorticosterone=0·5, and progesterone=0·02.

[The method appears to be a valuable and quick one. The qualitative results, however, were apparently derived from experiments carried out at different times against the same control group of rats. It is not demonstrated that the same degree of cold, for instance, will always give the same reduction of the adrenal ascorbic acid, either in the same rats on different days or in different rats on the same day.]

Peter C. Williams

2146. **Treatment of Simmonds's Disease with Testosterone Propionate.** (Tratamento da síndrome de Simmonds pelo propionato de testosterona)

J. SCHERMANN and R. FARIA. *Arquivos de Clínica* [*Arch. Clín.*] **4**, 328–342, May, 1947. 4 figs., 66 refs.

Dermatology

2147. **The Use of the Hormones in Dermatology**
M. M. HARTMAN. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **8**, 229–237, May, 1947. 21 refs.

Apart from specific effects the endocrine disorders may react indirectly on the skin: (*a*) through the autonomic nervous system; (*b*) by affecting the emotional state and aggravating or initiating psychosomatic disorders; (*c*) by modifying the allergic status. A summary of the uses of hormones in dermatology is given under 3 headings.

1. Skin disorders due to the deficiency or absence of a specific endocrine product responding to substitutive therapy: (*a*) Pigmentation in Addison's disease. (*b*) Myxoedema. (*c*) Urticaria and dermographia in dystrophia adiposo-genitalis. (*d*) Xanthoma diabeticorum. (*e*) Pruritus vulvae of the climacteric, senile vaginitis, and kraurosis vulvae. (*f*) Skin manifestations of diabetes mellitus and independent cutaneous " glycohistechia " (Urbach). Oestrogen therapy may be effective in cases of pigmentary disturbances at the menopause or in young women with amenorrhoea.

2. Skin disorders not due to a specific hormone deficiency but in which a hormone has a useful effect. Urticaria and angioneurotic oedema are improved temporarily by adrenaline and " pitressin ". Parathyroid hormone has an application in papular urticaria. Pitressin may relieve symptoms in zoster. Desiccated thyroid may be useful in xanthoma tuberosum, xeroderma and congenital ichthyosis, and seborrhoeic dermatitis. Oestrogens are given in the treatment of gonorrhoeal vulvo-vaginitis and in gonorrhoea and trichomonas vulvo-vaginitis after the menopause. Methyl testosterone can be used in chloasma gravidarum.

3. Skin disorders in which endocrine dysfunction may be a precipitating or aggravating factor. This group includes atopic dermatitis, urticaria, and acne. The author describes results of thyroid treatment in this group and discusses at length the relation to the gonadal hormones. *James Marshall*

2148. **" Gougerot's Triad ": Triad Consisting of Small Nodules of the Skin, Polymorphous Erythema, and Purpura.** (" Maladie trisymptomatique de H. Gougerot ": Trisymptome associant petits nodules dermiques, cocardes d'érythème polymorphe, purpura)
H. GOUGEROT. *Semaine des Hôpitaux* [*Sem. Hôp., Paris*] **23**, 1311–1315, May 28, 1947. 3 figs.

Since the 1914–18 war the author has observed 6 cases of a syndrome not previously described. The main features are: (1) erythemato-papular lesions 2 to 10 (rarely 20) mm. in diameter, sometimes annular or circinate, usually resembling erythema multiforme, but occasionally urticarial and rarely roseolar; (2) purpuric macules, 1 to 5 mm. in diameter, rarely larger; and (3), most important, little rounded nodules in the dermis, or dermis and hypodermis, 2 to 7 mm. in diameter, hard and well-defined, with no surrounding oedema, and causing no change in, or at most a little reddening of, the overlying skin. In exceptional cases there are larger nodules, 50 to 60 mm. in diameter, which, as they resolve, become seeded with smaller nodules. These principal elements are found all over the body, including the face, but mostly on the limbs, especially the legs, where there may be several hundred lesions. They appear in crops, clearing in 2 to 8 weeks without softening, abscess formation, ulceration (save in an exceptional case), or scarring.

The disease is chronic, lasting for years, with rare and inconstant febrile attacks with headache and joint pains, accompanied by exacerbation of the skin lesions. General health is maintained over the years, but patients are easily fatigued. Eventually the sufferer is enfeebled and loses more and more weight, but 1 patient is still alive after 20 years. In the first 3 cases a mitral valve murmur was heard, but the others showed no signs of endocarditis.

The author believes the disease to be a septicaemia, but no organism has yet been isolated. The skin lesions are produced by an allergic mechanism. Microbic emboli provoke nodule formation if they come to rest in the deep layers of the dermis and papular erythema if they reach the superficial layers, the skin being sensitized. The syndrome is compared and contrasted with infective endocarditis, where a much more serious general condition is associated with sparse cutaneous lesions.

Histological studies show: (1) that the lesions are always in the dermis; (2) that there is at this level an intense vascularity, or rather a capillarity; and (3) that the tissues locally are the seat of an intense necrosis, in which numerous polynuclear (mainly neutrophil) cells with normal or pyknotic nuclei are the essential elements.

Aetiology, pathogenesis, and prognosis are discussed in detail, and there are good illustrations, some in colour. All forms of treatment have so far been unsuccessful. Penicillin, 4,000,000 units, caused improvement, though there was subsequent relapse in 1 case, and it is intended to try this remedy again in the dosage used for infective endocarditis. The author concludes that this syndrome is related to infective endocarditis, multiform erythemata, and infective purpuras, and that it should be classified as a cutaneous allergid. *James Marshall*

2149. **A Method for Protection of Patients with Solar Urticaria**
L. RUBIN, P. L. BEAL, and S. ROTHMAN. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **8**, 189, April, 1947. 3 refs.

Two patients under treatment for solar urticaria with an antihistamine substance, " pyribenzamine ", noticed that the areas of skin normally exposed were more tolerant to sunshine than those parts usually covered.

The conclusion that exposure to sunlight under the protection of pyribenzamine produced local changes in the skin which themselves gave protection to the antigenic wave-lengths was confirmed by exposing the whole body surface of 1 patient, with the exception of the lower abdomen, to the irradiation of an artificial sun lamp daily, 50 mg. pyribenzamine being given three times daily. The time of exposure was gradually increased; after thirty-seven exposures the dose was reduced to 50 mg. twice daily, after forty-four to 50 mg. once daily, and after fifty-four the pyribenzamine was discontinued. Fourteen days after the drug had been discontinued, sensitivity tests to light on the exposed and unexposed parts of the abdomen showed that the irradiated parts acquired a tolerance more than 200 times greater than the covered parts. This effect is due to pigmentation and/or thickening of the horny layer. No immunological desensitization mechanism is involved.

H. R. Vickers

2150. **Group Sensitivity to Local Anesthetics. Confirmation of the Possibility of its Occurrence and Demonstration that it does not Necessarily always take Place**
M. J. STRAUSS. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **8**, 403–407, June, 1947. 7 refs.

2151. **Skin Sensitization to Vesicant Agents of Chemical Warfare**
M. B. SULZBERGER, R. L. BAER, A. KANOF, and C. LOWENBERG. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **8**, 365–393, June, 1947. 3 figs., 69 refs.

2152. **Tropical Phagedenic Ulcer (Vincent's Ulcer)**
H. BLANK. *American Journal of Tropical Medicine* [*Amer. J. trop. Med.*] **27**, 383–398, May, 1947. 5 figs., Bibliography.

Tropical phagedenic ulcer is defined as a specific acute ulcerative skin lesion with characteristic slough, containing numerous fusiform bacilli and spirochaetes in its early stage, which may develop later into a chronic non-specific ulcer; it is widely distributed in tropical and sub-tropical countries.

The lesions occur almost exclusively in the legs and below the knee and usually at the site of some injury, often of a minor nature. Typically, in the acute stage the ulcer is painful, oval or circular, of large extent, foul smelling, and filled with a gangrenous slough. The edges are irregular and often undermined, and the lesion may involve tendon and even bone. [Cases of spontaneous fracture of the tibia and fibula have been described.] Europeans and well-to-do natives are rarely affected; in fact, the condition has been described as a "poor man's disease". Preponderance of evidence shows that this condition is caused by infection with fusiform bacilli and spirochaetes in a patient suffering from a vitamin-B deficiency and usually debilitated by chronic disease—such as syphilis, yaws, helminthiasis—and general malnutrition. Desert sores, cutaneous diphtheria [some observers consider these two conditions identical], cutaneous leishmaniasis, and syphilitic gummata must be differentiated.

Treatment of the general condition is most important—correction of dietetic deficiencies and treatment of yaws, syphilis, or helminthiasis. [The abstracter has found arsenicals (neoarsphenamine) to be of benefit in East African cases, possibly owing to the local prevalence of yaws, but many observers do not consider arsenicals to be of value.] To arrest the phagedenic process antiseptics, débridement and gentle curettage, rest, local applications of sulphonamides and of pastes such as "bipp" and "zipp" are of value. Copper sulphate has also been recommended. At a later stage skin grafting will assist growth of epithelium, but it will usually be necessary first to curette the hard tissue at the base of the ulcer. More recently, penicillin given locally and by injection has been found of great value.

A case of typical tropical ulcer of the leg in a young Chinese male who was treated with penicillin is described in detail. The patient received 360,000 units in eighteen doses given intramuscularly every 3 hours; he had no other treatment except an adequate diet. One week after cessation of penicillin administration the ulcer was clean and healing; 10 weeks later, without any particular local treatment but with administration of vermifuges for ascaris and ancylostoma, a multivitamin supplement, and iron, the ulcer was healed, no skin graft being needed. The author thinks that penicillin will probably become the treatment of choice.

C. F. Shelton

2153. **Undecylenic and Propionic Acids in the Prevention and Treatment of Dermatophytosis**
M. B. SULZBERGER and A. KANOF. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph., Chicago*] **55**, 391–395, March, 1947. 4 refs.

This is a report of studies on the efficiency of certain fatty acids and their salts in the prophylaxis and treatment of dermatoses suggestive of fungous infection of the feet. Comparable groups of individuals were treated with different preparations. In some cases of equal infection in both feet, the two feet were treated with different applications, and the results compared (the "Hart's Island paired comparison method"). In a series of 70 cases undecylenic acid-undecylenate powder proved to be the most effective preparation of those employed. From further extensive clinical trials in subtropical climates it appeared that this preparation in powder form reduced the incidence of dermatophytosis by 85%.

John T. Ingram

2154. **Treatment of Mycotic Infections by Inhibiting Respiration of Dermatophytes**
F. A. DOLCE and W. J. NICKERSON. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph., Chicago*] **55**, 379–384, March, 1947. 6 refs.

Laboratory investigations have shown that the oxygen consumption and consequently the growth of fungi can be inhibited by variation of *p*H or of salt concentration or by the addition of various organic and inorganic

substances. Zinc chloride (1% in alcoholic solution) was found to be an effective inhibitor in dilute concentration, and the authors have examined its clinical value.

In the American Army Air Force 11·8% of all dermatological cases were of superficial mycotic infections. A group of 45 patients were treated, including patients with ringworm infection of toes, of groin, and of smooth skin and 2 children with small-spore ringworm infection of the scalp. The results of treatment with zinc chloride were not impressive; only 6 cases appeared to be cured after 20-days' treatment, and this included no case of ringworm of the feet. Some acute infections were aggravated and patients developed lymphangitis, cellulitis, and secondary "id" eruptions. *John T. Ingram*

2155. **Topical Use of Penicillin in Treatment of Pyoderma**
B. J. HOFFMAN. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph., Chicago*] **55**, 630–632, May, 1947. 2 refs.

The topical use of a solution of 800 units per ml. of penicillin in isotonic saline was found effective in controlling cutaneous pyogenic infection. It was superior to controls of penicillin of the same strength or of 5% sulphadiazine in a water-soluble base. A wet dressing of penicillin solution was applied twice a day, the part being kept in a Bunyan bag to prevent evaporation. Contact dermatitis was not uncommon after 4 to 5 consecutive days of wet dressings and 6 to 10 of penicillin ointment, but could be minimized by discontinuing treatment for 1 to 2 days after 4 days of wet dressings and 6 days of ointment. *G. A. Hodgson*

2156. **Melanotic Prurigo (A New Form of Prurigo).** (Prurigo melanótico (Una nueva forma de prurigo))
L. E. PEIRINI and J. M. C. BORDA. *Revista Argentina de Dermatosifilología* [*Rev. argent. Dermatosif.*] **31**, 3–32, April, 1947. 21 figs., 26 refs.

2157. **The Treatment of Dermatitis Venenata (Rhus) by Cryotherapy. (Preliminary Report)**
M. M. ROBINSON. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **8**, 239–243, May, 1947. 10 refs.

Dermatitis due to contact with plants of the *Rhus* family is a self-limited disease. The duration is usually from 1 to 3 weeks, but may be several weeks longer. The treatment here described shortens the period to a maximum of 7 days with relief of symptoms after 1 or 2 days. The treatment was first described by a physical chemist who found workers in his plant curing poison-ivy dermatitis by swabbing the skin with a cotton sponge soaked in liquid air. The author found liquid air an effective but not, of course, a practical method. Carbon dioxide-ether slush was also efficient but difficult to apply. The simplest and most effective method was to spray the skin with ethyl chloride, as for local analgesia, until the skin frosted and for a few seconds longer, when it became hard to the touch. Spraying was repeated at 24-hour intervals. A day after the spraying the skin was very red; some vesicles had been absorbed while others had ruptured and scabbed. The treatment is relatively painless and reduces itching. Care must be taken to avoid anaesthesia when treating the face. Five cases (out of 101) did not respond well because of secondary infection. The average duration of the condition was 5 days with three treatments. Promising results were obtained with small numbers of cases of other vesicular dermatoses, notably herpes simplex and zoster.
James Marshall

2158. **Photosensitization in the Treatment of Psoriasis**
E. EPSTEIN. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **8**, 203–207, April, 1947. 3 refs.

One of the most popular methods of treating psoriasis is by the simultaneous use of photosensitizing agents and ultraviolet radiation. Different agents are employed, and this article is an attempt to assess their value. Series of patients were treated by five different methods, and the results of treatment assessed as "cleared, marked improvement, moderate improvement, and poor"; by combining the figures for "cleared" and "marked improvement", an "effective rate" for the method employed was obtained.

Ultraviolet light, sulphanilamide, and crude coal-tar paint were employed together. The lesions were painted on the morning of the day before and also the morning of light treatment with a liquid containing 10% crude coal tar and 20% acetone in benzine; sulphanilamide gr. 5 (0·3 g.) was given by mouth four times on the day before treatment. Eleven patients were treated with an "effective rate" of 90·9%. Nine patients received irradiation alone, with an "effective rate" of 22·2%. Four patients received ultraviolet light irradiation and sulphanilamide, a number too small to be conclusive, but the "effective rate" in these was 100%. Eleven patients were treated by irradiation and tar painting, with an "effective rate" of 81·7%.

The author points out that *x*-ray therapy for a chronic relapsing disease has its dangers, but if it is carefully controlled the dangers are probably less than those of administration of sulphonamides; 23 patients were treated by *x* rays, with an "effective rate" of 82·5%.

From the results of the trials the author concludes that psoriasis can be controlled effectively by the combined use of ultraviolet light and a photosensitizing substance; however, recurrences are as frequent as with other methods of treatment and, without photosensitization, ultraviolet light is comparatively ineffective.
H. R. Vickers

2159. **Basal Cell Epithelioma in a Psoriatic Patch**
A. G. FRANKS and J. L. BARNER. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph., Chicago*] **55**, 375–378, March, 1947. 2 figs., 7 refs.

2160. **Scleroma: An Etiological Study**
M. G. LEVINE, R. E. HOYT, and J. E. PETERSON. *Journal of Clinical Investigation* [*J. clin. Invest.*] **26**, 281–286, March, 1947. 21 refs.

2161. **Treatment of Mycosis Fungoides with Nitrogen Mustard**
H. H. HENSTELL and J. N. TOBER. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **8**, 183–188, April, 1947. 6 figs., 4 refs.

Following the favourable reports of Gilman and Philips and others on the use of nitrogen mustards in the treatment of Hodgkin's disease and related lymphomata, the authors treated a case of mycosis fungoides with methyl - bis - (β-chloroethyl)amine hydrochloride. The patient was a 67-year-old white woman who, in August, 1945, was found to be suffering from mycosis fungoides, the diagnosis being confirmed by biopsy. She was treated with total body spray irradiation in divided dosage, a total of 300 r being given to the body and 800 r to the chest. She then had 1 g. sodium thiosulphate intravenously weekly for 11 months and afterwards diphtheria toxoid 1 ml. intramuscularly weekly for 2 months without any improvement.

In October, 1946, the whole skin with the exception of the face and scalp was covered by an irritable generalized papular eruption, the papules being 2 to 3 mm. in size and raised 1 to 2 mm. The entire skin was thickened, brawny, red in colour, and showed recent scratch marks. Over the right breast and the posterior aspect of the right chest was an eczematoid vesicular eruption with some weeping. A few small lymph nodes were palpable in the cervical and inguinal regions. The only abnormal laboratory findings were a slight increase of eosinophils and eosinophilic myelocytes in the sternal marrow smear; biopsy of the skin showed the changes of mycosis fungoides.

Methyl-bis-(β-chloroethyl)amine hydrochloride, 5 mg., dissolved in 5 ml. of distilled water was injected into the tubing of an infusion of normal saline in November, 1946, and this dose was repeated on the two following days. Four days after the treatment started the papules, patches of infiltration, and pruritus began to disappear. At the end of a week the skin appeared to be normal except for the vesicular lesions which became herpetic. Biopsy taken on the ninth day from the same area as the previous biopsy showed that the intense infiltration of the earlier sections had gone. One month afterwards the herpetic lesions had almost entirely disappeared. This paper is a preliminary report and later reports of this case and others will be published. *H. R. Vickers*

2162. **A New Method of Treating Capillary Haemangiomas.** [In English]
G. JÖNSSON. *Acta Chirurgica Scandinavica* [*Acta chir. scand.*] **95**, 275–285, March 15, 1947. 4 figs., 7 refs.

After a general review of the various types of haemangiomata the results of treatment of the capillary haemangioma are appraised and it is concluded that " apart from excision the results of the methods enumerated have been such that most authors are of the opinion that capillary haemangiomas had better be left untreated ". The present author then relates a simple, satisfactory method of treatment which he has tried on 17 cases at Eksjo Hospital with good cosmetic results. The method consists in trying to remove or destroy the capillaries in the surface layers of the skin by rubbing the haemangioma with sand-paper while leaving the subcutis intact. Procaine (1% to which one drop of 1 in 1,000 adrenaline is added to 10 ml. of the solution) is injected so that an oedematous cushion is formed under the lesion. The surface of the haemangioma is then carefully rubbed with ordinary sterilized sand-paper (sizes No. 2 to No. 5). In some cases small wooden blocks covered with sand-paper have been used. The bleeding is profuse and compression must be applied the whole time. Deep rubbing into the cutis should be avoided and, of course, the subcutaneous fat should never be visible. The raw surface is covered with a sulphathiazole dressing, which is not changed for 5 or 6 days; a sulphathiazole ointment is then applied. Complete healing always took place within 10 days. All cases of capillary haemangioma are not equally well suited for this treatment; the best results are seen if the colour is of the darkest possible red, preferably with a tinge of blue. A good result is only obtained if the haemangioma can easily be emptied of blood by compression or stroking—that is, if it is very superficial. If no result has been achieved after the haemangioma has been rubbed on two occasions further treatment by this method is useless. Of the 17 cases treated there were good results in 10 and moderate results in the other 7.
Zachary Cope

2163. **Recurrent Bullous Eruption of the Feet**
E. A. COCKAYNE. *British Journal of Dermatology and Syphilis* [*Brit. J. Derm.*] **59**, 109–112, March, 1947. 11 refs.

Recurrent bullous eruption of the feet, appearing only in warm weather, in a third London family is described and compared and contrasted clinically and histologically with the condition reported in other families. The abnormality is a conditional dominant. So far it is only known in the heterozygous state. In most of the families, affected males outnumber affected females, and there is an excess of affected over normal individuals. The author regards the condition as a definite entity, possibly an allelomorph of one or more of the described forms of epidermolysis bullosa. *G. B. Mitchell-Heggs*

2164. **Acanthosis Nigricans Juvenilis Associated with Obesity. Report of a Case, with Observations on Endocrine Dysfunction in Benign Acanthosis Nigricans**
S. S. ROBINSON and S. TASKER. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph., Chicago*] **55**, 749–760, June, 1947. 5 figs., 16 refs.

2165. **Estrone and Alpha-estradiol, Applied Locally, Ineffective in Reducing Facial Hypertrichosis**
W. WHITAKER, F. J. STODDARD, J. N. GREKIN, and L. GOFORTH. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **9**, 49–54, July, 1947. 8 refs.

Venereal Diseases

2166. **Relation of the Size of the Inoculum and the Age of the Infection to the Curative Dose of Penicillin in Experimental Syphilis, with Particular Reference to the Feasibility of its Prophylactic Use**

H. EAGLE, H. J. MAGNUSON, and R. FLEISCHMAN. *Journal of Experimental Medicine* [*J. exp. Med.*] **75**, 423–440, April 1, 1947. 2 figs., 15 refs.

Material used in this study consisted of the Nichols strain of *Treponema pallidum* passaged intratesticularly. Inocula were obtained by emulsification of rabbit testicular chancre in 50% rabbit serum and dilution to obtain concentrations of 10^6, 10^4, and 10^2 organisms per ml., 0·2 ml. of the appropriate dilution being injected intracutaneously or intratesticularly. Penicillin, in one single intramuscular dose of a suspension in oil and beeswax, was administered 4 hours, 4 days, or 2 weeks after inoculation. At each of these intervals groups of 4 to 11 rabbits were given increasing doses to determine the abortive dose of penicillin required. This latter dose was compared with that necessary to cure animals treated 6 weeks after inoculation and after a lesion had developed. Administration of relatively small doses of penicillin 4 days after inoculation aborted the disease; the preventive dose (P.D.) varied with the size of inoculum and with the age of the infection. Thus, in animals inoculated with 20, 2,000, and 200,000 spirochaetes and treated 4 days later, 200, 500, and 3,500 units per kilo, respectively, were needed to protect half the animals, and the corresponding PD 90 dosages were 500, 2,000, and 16,000 units per kilo. With a fixed intratesticular inoculum the PD 50 of penicillin remained at a constant level for 4 days. By the end of the second week more than seven times the dosage was required, while by the sixth week, after the appearance of the chancre, more than thirty times the amount was necessary to produce the same results.

The authors consider that administration of penicillin in one single intramuscular dose shortly after contact might prove a successful form of prophylaxis in human infection. In man and rabbit renal clearance of penicillins F, G, and X is maximal, the blood level falls at essentially the same rate, and after intramuscular inoculation there are comparable rates of absorption. Equal dosages per kilo in both species should, therefore, produce similar results on the spirochaete. Thus, in the average adult, a single intramuscular injection of 15,000 units in peanut oil and beeswax after, say, 4 days' exposure might effectively abort infection. Even oral administration of three to five times this dose should prove effective. This suggests a new approach to the prophylaxis of syphilis, for if the spirochaete multiplies as slowly in man as it does in the rabbit a single dose of penicillin, orally or intramuscularly, should even abort the infection if it is given some days after exposure.

Margaret Buchanan

2167. **Effect of Penicillin on Serology of Late and Latent Syphilis. (A Study of 120 Cases Followed for Six Months or More)**

R. R. WILLCOX. *Lancet* [*Lancet*] **2**, 8–10, July 5, 1947. 3 refs.

The author studied the effect of penicillin on the serology of 120 military personnel treated at an Army hospital for congenital, latent, and late syphilis. The comparatively short time of 6 months' observation or more was sufficient to detect the trend of the early pathological changes in response to penicillin. A qualitative Wassermann and a quantitative Kahn test were carried out on the blood serum once a month for the first 6 months, quarterly for the following year, and 6-monthly for a further year. The cerebrospinal fluid (C.S.F.) was examined before penicillin was given and again after 6 months. It will again be examined after 2 years.

The cases were divided into 4 clinical groups: congenital syphilis, 25 cases; early latent syphilis (known infection within 5 years), 33 cases; latent syphilis (duration unknown), 34 cases; and late symptomatic syphilis, 28 cases. Serological results are ingeniously arranged into 4 groups of varying stability: (1) low declining titre, (2) high fluctuating titre, (3) high fixed titre (completely resistant to previous treatment), and (4) high titre of unknown stability (not previously treated). Groups 1 and 2, both with fluctuating titres after previous treatment, responded most favourably (74·2 and 94·4%), while group 3, with fixed titre to arsenic and bismuth, gave little evidence of further improvement (16·1%). Group 4, a mixture of the other groups, showed indifferent success (27·5%). The results in cases with an initially low titre were better after 6 months but the improvement was not maintained and an appreciable number of patients relapsed later. The improvement continued for 9 or 12 months in the cases with a high fluctuating titre. Latent syphilis of recent origin responded most, while late syphilis and congenital syphilis responded least. The C.S.F. was abnormal in 18 cases; only 9 cases of the 15 examined had improved 6 months later, and only 3 among the 9 showed similar improvement in the blood. In this small series the findings in the blood and in the C.S.F. were not parallel.

As the author states, the analysis is confused because many patients had been treated with arsenic and bismuth before penicillin was given. Again, some patients were given arsenic and bismuth after penicillin; failure in these cases, however, would imply failure after penicillin alone.

Patients had a total dosage of 2,400,000, 4,000,000, and 4,800,000 units of commercial penicillin in aqueous solution in 3-hourly injections of 40,000 units. Six of the 25 congenital syphilitic patients improved. All of the 33 cases with early latent syphilis had had arsenic

and bismuth previously; 26 (78·8%) improved. As would be expected, results were less satisfactory in patients with latent syphilis of unknown duration: 16 out of 34 responded. At the end of 6 months only 8 (28·6%) of the 28 patients with late, mostly gummatous, syphilis had improved.

[The marked difference in the total dosage of penicillin in the three schedules of treatment must affect the value of the comparative figures in this study to a considerable degree; accurate comparisons can hardly be made since the dosage received by the various categories of patients is omitted.] *T. Anwyl-Davies*

2168. **Penicillin in the Treatment of Experimental Syphilis of Rabbits. I. The Therapeutic Activity of Penicillin in Single and Multiple Doses in Isotonic Solution of Sodium Chloride and Peanut Oil–Beeswax by Intramuscular Injection**

J. A. KOLMER. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph., Chicago*] **55**, 741–748, June, 1947. 5 refs.

Rabbit experiments were performed with two specimens of penicillin of a potency of 544 and 1,624 units per mg. and of a G content of 88 and 92% respectively. These penicillins, dissolved in isotonic saline solution, were compared in their effect on rabbit syphilis with the same penicillins suspended in a mixture of arachis oil and 3% beeswax at a concentration of 10,000 units per ml. All rabbits were inoculated intratesticularly with the Nichols strain of *Treponema pallidum* and all developed orchitis positive on dark-field examination 5 to 6 weeks later. Treatment was then instituted and dark-field examinations were performed daily for 3 days and thereafter weekly for 10 weeks; at the end of this time the popliteal lymph nodes were inoculated into the testicles of fresh animals and these were observed for a minimum of 4 months.

Two rabbits were each given single injections of both penicillins in saline solution in doses of 10,000, 30,000, and 100,000 units per kilo body weight. Though preliminary dark-fields tests became negative, all 12 rabbits later relapsed and showed positive lymph-node transfers. With the same doses of penicillin in oil–wax, however, a cure was obtained in 3 out of 4 receiving a single injection of 10,000 units per kilo and in all 8 receiving the larger amounts.

When injections were given daily multiple doses of 1,000, 5,000, and 25,000 units per kilo were employed once daily for 8 days. With saline solution, temporary improvement with later relapse was noted in all 4 on the lowest dose and in 3 with the total dose of 40,000 units; no improvement was noted with the total dose of 200,000 units. With penicillin in oil–beeswax 3 out of 4 rabbits were cured by the lowest dose and all by greater doses. With multiple injections of the same doses given twice daily over 8 days, 3 out of 4 rabbits responded to the lowest doses of saline solution and all to the higher doses, while with penicillin in oil–beeswax all 12 animals were cured. Thus the results with penicillin in oil–beeswax in rabbit syphilis show a decided improvement on those with penicillin in saline solution. *R. R. Willcox*

2169. **Treatment of Early Acquired Syphilis with 600,000 units of Sodium Penicillin**

D. C. SMITH, W. H. KAUFMAN, and J. C. SHAFER. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph., Chicago*] **55**, 644–649, May, 1947. 9 refs.

Thirty-four patients, 2 with serum-negative, 8 with serum-positive primary syphilis, and 24 with secondary syphilis, received a total of 600,000 units of different brands of commercial sodium penicillin in saline solution; it was administered in thirty 3-hourly intramuscular injections. All the patients have been studied for at least a year, 29 for 18 months, 20 for 21 months, and 14 for 2 years or more. There were 21 female and 30 negro patients.

A Herxheimer reaction was obtained in 13 and there were no toxic effects. In 8 cases observed *Treponema pallidum* disappeared from the initial lesions in 8 to 23 hours. Chancres healed in 12 to 47 days and secondary lesions in 10 to 56 days, although in 1 case lesions persisted until a relapse after 97 days. The 2 patients with serum-negative primary syphilis were still in a satisfactory condition after 548 and 760 days respectively. Seven of the 8 serum-positive primary patients were well after 419 to 715 days, but there was 1 with muco-cutaneous lesions at 124 days. Ten of the 24 secondary cases also relapsed; 7 with muco-cutaneous lesions at 97 to 347 days (average 209 days) and 3 with serological relapses at 135 to 376 days. Five of these relapses occurred at periods under 6 months and the remainder after that time. In addition 3 other patients still show some degree of serum-resistance after 383 to 627 days. Thus, only 20 (58·8%) are regarded as showing favourable results. *R. R. Willcox*

2170. **Observations on the Therapeutic Efficacy in Experimental Syphilis of Calcium Penicillin in Oil and Beeswax and their Bearing on its Use in Man**

H. EAGLE, H. J. MAGNUSON, and R. FLEISCHMAN. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **31**, 246–256, May, 1947. 2 figs., 4 refs.

These experiments were undertaken to show that a single injection of penicillin in beeswax–oil suspension resulting in a prolonged low blood level was more effective in experimental syphilis in the rabbit than a single injection of an aqueous solution and as effective as multiple small injections. The effect of different concentrations of beeswax in oily penicillin is also studied, as well as the optimum method of administering oil–wax preparations in experimental syphilis.

The rabbits were treated 5 to 7 weeks after intratesticular inoculation, proof of cure being confirmed by popliteal lymph-node transfers into two normal animals 6 months after treatment. Suspensions of calcium penicillin in peanut oil were prepared containing: (*a*) no beeswax; (*b*) beeswax 3% by volume; (*c*) beeswax 6% by volume, the infected rabbits receiving 4 successive daily injections of the different preparations. The total dosage of penicillin necessary to cure 50% of the animals fell from 39,000 to 8,000 to 3,500 units per kilo of body weight

as the concentration of beeswax was increased from 0 to 3 to 6% by volume. The dosage necessary to cure 90% of the animals fell correspondingly from 80,000 to 16,000 to 8,000 units per kilo. Oily suspensions of penicillin without beeswax were only slightly more effective than aqueous solutions similarly administered.

The effect of five different schemes of treatment with penicillin in oil and beeswax is shown in one table and the relative therapeutic efficacy of penicillin in aqueous solution and in oil–wax suspension in another table. It is noteworthy that the superiority of the oil–wax preparations over the watery solution becomes less marked when treatment is prolonged, and that the margin of difference between the two preparations narrows as the number of injections is increased and the dose of penicillin per injection is decreased. High penicillin blood levels do not appear to be necessary for the cure of syphilis, and, as would be expected, the maximum wastage of penicillin occurs with large injections of an aqueous solution. The authors conclude that their observations in animals would probably find a parallel in the treatment of human syphilis or acute bacterial infections.

[This is an important paper which should be read in the original to be appreciated.] *G. L. M. McElligott*

2171. **The Local Chemical Prophylaxis of Experimental Syphilis with Phenyl Arsenoxides Incorporated in Ointments and in Soap**

H. EAGLE, H. J. MAGNUSON, and R. FLEISCHMAN. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **31**, 257–263, May, 1947. 18 refs.

These workers in their laboratory at Johns Hopkins University have previously shown that solutions of various phenyl arsenoxides in propylene glycol when applied to a skin incision previously inoculated with *Treponema pallidum* can prevent rabbits from developing syphilis. In this study they show that ointments compounded with these arsenicals are not so effective as are the solutions in propylene glycol, whether the ointments are made up from the finely divided dry arsenical suspended in a fatty base or from arsenical solutions homogenized in an aqueous one; only occasionally were more than three-quarters of the animals protected, even when the arsenical concentration given was as high as 0·4%. Rather better results were achieved when the arsenicals were dissolved in a soap solution (5% potassium oleate in water). Results compared favourably with those obtained with the same compound in propylene glycol. It is surprising to learn that the soap solution alone was wholly inert.

The authors consider that arsenical prophylaxis deserves trial in the human subject, and that reliable data could be obtained from a relatively small study in a group of volunteers deliberately inoculated with a known spirochaetal suspension and subsequently treated by one or more prophylactic procedures. [They do not suggest where these "volunteers" are to be found, though a promise of remission of sentence or even of certain privileges might possibly produce them from among the inmates of State penitentiaries.]

G. L. M. McElligott

2172. **Clinical Nephropathies in Early Syphilis**

E. W. THOMAS and M. SCHUR. *Archives of Internal Medicine* [*Arch. intern. Med.*] **78**, 679–686, Dec., 1946. 12 refs.

Syphilitic involvement of the kidneys, especially in the secondary stage, has long been recognized but is very rare. In only 12 (less than 0·3%) of all the cases of secondary syphilis treated by the authors at the Bellevue Hospital, New York, in 1940–6 were there markedly abnormal urinary findings which responded rapidly to antisyphilitic treatment. Ten of the patients were women. The 3 cases described in detail occurred in young negroes [but there is no indication whether syphilitic renal disease is relatively more frequent in negroes].

Albuminuria may be mild or very heavy with numerous casts; red blood cells are present in variable numbers and may cause frank haematuria. The cases can be grouped into those of nephrosis and nephritis, but the dividing line is indistinct. In early syphilitic nephrosis there is heavy albuminuria (10 to 30 g. daily), usually with numerous waxy casts but few or no red blood cells, and oliguria. Renal function is rarely impaired, and the non-protein nitrogen of the blood is not raised. Plasma protein level is normal and oedema is slight or absent in most cases. Ten of the 12 were classified as cases of nephrosis rather than of nephritis. The patients have usually no subjective complaints, and the albuminuria is found on routine investigation. The abnormal urinary findings disappear rapidly with antisyphilitic treatment, and only 1 patient gave a Herxheimer reaction, in spite of which the renal disturbance quickly improved.

Early syphilitic nephritis is distinguished from the nephrotic syndrome chiefly in that there is a relatively mild albuminuria with a much greater haematuria. Two cases are described, of which one simulated the focal rather than the diffuse type of glomerulonephritis, with heavy haematuria, moderate albuminuria, and numerous granular casts, but no subjective complaints, hypertension, anaemia, or loss of renal function. The other patient had a typical attack of diffuse glomerulonephritis with moderate albuminuria, mild haematuria, hypertension, some anaemia, and impaired renal function. It was associated with secondary syphilis, and both conditions responded rapidly to penicillin. The authors admit that syphilis may not have been the true cause of the nephritis, but in view of the parallel response to specific therapy it appears more than likely. In contrast, 3 cases are mentioned in which secondary syphilis was contracted by patients known to have nephritis, and in whom there was no response of the renal condition to antisyphilitic treatment. These early syphilitic nephropathies do not appear to leave any permanent renal damage.

E. G. Sita-Lumsden

2173. **Cross Immunity in Experimental Syphilis, Yaws, and Venereal Spirochetosis of Rabbits**

T. B. TURNER, C. MCLEOD, and E. L. UPDYKE. *American Journal of Hygiene* [*Amer. J. Hyg.*] **46**, 287–295, Sept., 1947. 9 refs.

2174. **A Comparison of the *in Vitro* Susceptibility of the Gonococcus to Penicillins G and X**
M. J. ROMANSKY and E. V. D. ROBIN. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **31**, 271–276, May, 1947. 7 refs.

The susceptibility of different strains of gonococci to various preparations of penicillin was tested *in vitro* by the serial dilution tube and the plate methods. The two methods gave parallel results and therefore both are considered reliable. The plate method is technically superior because several strains can be tested on the same plate and all plates remain under standard conditions throughout. Of 53 strains tested 79·2% were susceptible to 0·0156 to 0·0313 units of commercial penicillin, while in another group of 41 strains 80% were susceptible to 0·02 units per ml. No difference in susceptibility to commercial penicillin was noted between strains from untreated and sulphonamide-fast patients. Forty-one strains were tested against penicillin G and three batches of penicillin X; no difference in susceptibility was noted. *S. M. Laird*

2175. **The Treatment of Gonorrhea with Streptomycin**
B. D. CHINN, L. E. PUTNAM, S. R. TAGGART, and R. P. HERWICK. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **31**, 268–270, May, 1947. 4 refs.

The possible large-scale appearance of penicillin-resistant gonorrhoea (laboratory and clinical reports of this condition are quoted) led the authors to assess the value of streptomycin against the gonococcus. A pilot study of 4 cases gave encouraging results, and a larger series was treated to determine optimum dosage. A single dose of 0·5 g. produced cures consistently in 25 cases, as did 0·4 g. and 0·3 g. in further series of 10 and 15 patients respectively. Twenty patients were cured out of a series of 22 receiving 0·2 g., but the other 2 responded to a further injection of 0·2 g. The streptomycin was given in aqueous solution as a single injection into the gluteal muscle; reactions were negligible. Some patients complained of pain for several hours at the site of injection. In 2 patients typical Herxheimer reactions occurred, and both subsequently gave a positive response to serological tests for syphilis. While penicillin at present remains the treatment of choice for gonorrhoea, it is valuable to know that, if penicillin-resistance develops, streptomycin should prove an effective alternative. *S. M. Laird*

2176. **Treatment of Acute Gonococcic Urethritis with Single Subcutaneous Injections of Penicillin in Beeswax–Peanut Oil**
D. FROST, M. F. ALLENDE, W. M. M. KIRBY, and H. S. GINSBERG. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **31**, 300–303, May, 1947. 4 refs.

The report (*J. Amer. med. Ass.*, 1945, **129**, 940) that more regular absorption with prolongation of effective blood levels is achieved with the subcutaneous than with the intramuscular injection of penicillin–beeswax–peanut-oil mixtures led the present authors to test the former route of administration. A standard commercial penicillin–beeswax–peanut-oil mixture containing 300,000 units of penicillin per ml. was used. Of 360 soldiers with acute gonorrhoea receiving 1 ml. of the mixture subcutaneously in the outer aspect of the thigh, 200 were studied for a minimum of 21 subsequent days. Observation was clinical, and by smear and cultural examinations on the seventh, fourteenth, and twenty-first days after treatment. Cure was achieved in 177 patients (88·5%); the authors did not consider this result superior to those obtained by similar treatment given intramuscularly. [No studies of the blood levels achieved by either route are mentioned.] Indurations and nodules formed in 10% of patients treated by subcutaneous injection, and 3 patients developed sterile abscesses. These reactions were most marked in patients receiving the injection into the skin, and were least likely to occur with deep subcutaneous injection. *S. M. Laird*

2177. **Elephantiasis of the Penis and Scrotum and Lymphogranuloma venereum Infection.** [In English]
W. E. COUTTS. *Dermatologica* [*Dermatologica, Basel*] **93**, 337–350, 1946. 1 fig., 35 refs.

In West Africa and other tropical areas, where lymphogranuloma venereum and filariasis exist side by side, it is common to ascribe penile and scrotal oedema to the latter rather than to the former condition. This article describes 32 cases observed between 1931 and 1945 in Chile, a country where filariasis is unknown. Twenty of these were investigated in hospital, and in the author's view lymphogranuloma venereum was proved definitely to be the cause in 18 and a probable cause in the remaining 2 cases.

The ages of the 20 patients varied from 24 to 64 years, 11 being over the age of 40. Fourteen had had inguinal adenitis a few months to 27 years previously (average 7·9 years); 1 of these patients had undergone bilateral inguinal adenectomy. Four others gave a history of previous venereal disease, and a positive Frei test was obtained in 12. In 3 the elephantiasis was concomitant with a rectal stricture, while urethrogenous forms of lymphogranuloma venereum as manifest by urethral stricture, urinary fistulae, or infiltrative lesions of the posterior urethra—were suspected in 4. Extensive proteiform skin lesions of the gluteal region and lower limbs were noted in 2, from 1 of whom a potent Frei's antigen was prepared. Eye fundus changes, as previously described in this condition, were noted in 6 patients and virus forms were found in 13 out of 14 biopsy specimens examined.

While positive serological tests for syphilis were obtained in 7 cases, this disease is not regarded as responsible for the oedema. With the intense infiltration of the scrotum spermatogenesis is impaired and azoospermia was found in 3 out of 4 patients examined. The only available treatment is plastic surgery with removal of as much as possible of the elephantoid tissue. In some cases this proved satisfactory, but in others it was followed by a gradual recurrence. *R. R. Willcox*

Genito-Urinary Disorders

2178. **Successful Treatment of Lipoid Nephrosis by Veyre's Method (Intravenous Injections of Dilute Hydrochloric Acid).** (Néphroses lipoïdiques traitées avec succès par la méthode de Veyre (injections intraveineuses d'acide chlorhydrique dilué))

C. LIAN, F. SIGUIER, and A. SARRAZIN. *Bulletins et Mémoires de la Société Médicale des Hôpitaux de Paris* [*Bull. Soc. méd. Hôp. Paris*] **63**, 368–384, May 16 and 23, 1947. 3 figs., 17 refs.

Four cases of " lipoid nephrosis " which were successfully treated by the intravenous injection of dilute hydrochloric acid are reported; 3 of them in detail.

The patient in the first case, a man aged 31, had a long history of intermittent albuminuria before oedema developed. One month's high-protein, low-salt diet, with thyroid to the limit of tolerance (0·55 g. daily) produced only slight and temporary improvement. Three months later Veyre's treatment was given; diuresis began on the third day and on the fourth alkali reserve was 50 vols. %. At the end of the course, oedema had resolved, but albuminuria persisted. Three months later the patient was back at work and feeling well.

In the second case, a man aged 24, 2 months' low-salt diet caused only a slight initial improvement. He was given a high-protein diet, with Veyre's treatment, but without thyroid. Diuresis began after the sixth injection, and oedema resolved. Protein and doubly-refractive bodies disappeared from the urine. Blood cholesterol fell from 600 to 300 mg. per 100 ml.; serum proteins rose from 4·5 to 6 g. per 100 ml.; albumin/globulin ratio rose from 1·1 to 1·4. The patient returned to work as a commercial traveller and 3 months later he was well and free from oedema and albuminuria.

The third case, that of a girl of 13, is described as one of " typical pure lipoid nephrosis ". Low-salt diet produced no amelioration. She was given Veyre's treatment, with a high-protein diet, but without thyroid. Diuresis appeared after the eighth injection and lasted for a week, during which time the patient lost 1 kg. (2·2 lb.) daily, regaining her normal weight. Intermittent albuminuria persisted. The blood cholesterol fell from 800 to 260 mg. per 100 ml. and the serum proteins rose from 4·4 to 7·6 g. per 100 ml.

In the fourth case, that of a young ballerina with pure lipoid nephrosis, Veyre's treatment produced a " striking " clinical response, diuresis following the tenth injection, after only partial benefit from a high-protein, low-salt diet, and thyroid administration up to 860 mg. daily.

The authors' methods are as follows. Two solutions are used; a buffer of citric acid 21·008 g., normal sodium bicarbonate 200 ml., distilled water to the litre, and a solution of N/10 hydrochloric acid; 350 ml. of the former is mixed with 650 ml. of the latter. Ampoules of 10 ml. are sterilized by the intermittent method at 70° C. The *p*H of these solutions, adjusted to 2·5, is stable for several months in ordinary glassware. Daily intravenous injections of 10 ml. are given for 15 consecutive days. For the next 15 days phosphoric acid is given by mouth [dose not stated]. If the first course of injections produces an insufficient result, the course may then be repeated. It is advised that the first course should be completed even if a satisfactory response is obtained before the fifteenth day. The procedure is regarded as harmless in this dosage, the authors having had no complications in their own series, a finding in accord with the experience of Veyre *et al.* in Hanoi, Indo-China. Some local phlebitis may follow a series of injections in one vein. There has been no evidence of renal irritation.

In a detailed discussion of the effects of treatment the authors stress the great symptomatic improvement seen both in their own cases and in the Hanoi series, improvement usually greater in degree than the biochemical changes produced, although the blood and urine metabolites do move towards normal. There seem to be no contraindications to the use of Veyre's treatment in lipoid nephrosis. The authors advise it where classical treatment fails and also as an adjunct to it.

Intravenous hydrochloric acid was apparently first used by American workers (Shropshire, *Urol. cutan. Rev.*, 1934, **9**, 613) in the treatment of genito-urinary infections; these workers supposed the acid to exert a direct antibacterial effect. Veyre himself (*Rev. méd. franç d'Extreme-Orient*, 1943, Nos. 4, 5, and 6: *ibid.*, 1944, No. 6) believes that the acid works by virtue of its hydrogen ions, which stimulate the production of an unidentified substance in the blood, which increases the flow of cortin from the adrenals. The present authors quote various experiments demonstrating an increased chloride shift to the erythrocytes when hydrogen ions are introduced into the blood stream, and showing that this raises the osmotic pressure exerted by the red-cell albumin. This, they hold, draws salt and water from the tissues into the blood stream which is later excreted when the effect of the injection has passed off. The biochemical findings are summarized from 6 Hanoi cases published by Veyre, in which the longest follow-up was 5 months. Each case responded favourably.

[These 9 case reports are in themselves fairly convincing, but a larger series, with adequate controls, is clearly needed before the effectiveness of Veyre's treatment is established. While it may be true that an intravenous injection of hydrogen ion does increase the osmotic pressure of the red-cell albumin in the way the authors suggest, they have not established that the amount of hydrochloric acid they inject (0·65 millimol. per day) is enough to disturb the alkali reserve of the plasma sufficiently for the effect to have quantitative significance. Neither is it clear that a sufficient increase could occur in the osmotic pressure of red-cell albumin to compensate for the lowered osmotic pressure of the serum proteins in these cases. From the work on plasma infusions in nephrotic nephritis—for example, Brown *et al.*, *Brit. med. J.*, 1942, **1**, 515—it is clear that a diuresis may follow very varying increases in plasma osmotic pressure, and that the oedema may increase even when a rise in plasma osmotic pressure has been achieved. Change in osmotic pressure of plasma protein, let alone of red-cell albumin, is not the whole explanation.]

G. I. C. Ingram

Locomotor Disorders

2179. **Eosinophilia in Spondylitis Ankylopoietica.** (Die Eosinophilie bei Spondylarthritis ankylopoetica rheumatica)
A. Böni. *Schweizerische Medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **77**, 647–648, June 14, 1947. 4 figs., 10 refs.

Eosinophilia is most often observed in the early stages of spondylitis ankylopoietica. The number of eosinophils is not constant but varies between wide limits, as shown by specimen curves from 4 patients. Of 14 patients, 8 showed a marked eosinophilia at the end of their first course of treatment, while in 6 cases the count was normal. The erythrocyte sedimentation rate curve shows deviations similar to, but not parallel with, those of the eosinophil count. The appearance of a constant eosinophilia usually heralds the onset of a subjective and objective improvement in the patient's condition, even though the sedimentation rate may remain high. In the chronic stage of the disease the appearance of eosinophilia may again foreshadow an improvement in the condition, although the latter may be preceded by a temporary exacerbation of the disease process. *S. S. B. Gilder*

2180. **Bornholm Disease in the Tropics**
W. M. Jamieson and D. M. Prinsley. *British Medical Journal* [*Brit. med. J.*] **2**, 47–50, July 12, 1947. 4 refs.

Bornholm disease has a number of synonyms, mostly descriptive, such as " epidemic myalgia ", " devil's grip ", " epidemic myositis ", and " acute benign dry pleurisy ". Outbreaks have been reported from Northern Europe, U.S.A., Britain, Southern Australia, and Egypt; 35 cases were seen in Aden between August 17, and October 25, 1946, and with one exception were confined to Service personnel and their families.

The onset was abrupt, with pain, headache, and some fever as the three commonest features. The pain was either sharp or of a constrictive nature, always made worse by respiratory effort; there was no position in which all patients felt most comfortable. Pain started in the epigastrium in 8 cases, along the right costal margin in 6, and along the left costal margin in 4. Pain was referred in 11 cases to shoulder-tip, interscapular region, or umbilicus to groin. It lasted usually from 3 to 7 days, once for as long as 23 days. Headache was present in 18 cases; often excruciating, it lasted up to 4 days, leaving the patient with a dull ache for several more days. There was fever at the onset in all cases except 1; the temperature was not usually above 100° F. (37·8° C.), but the highest reached was 105° F. (40·5° C.). Other symptoms complained of were sore throat, anorexia, nausea, vomiting, giddiness, and diarrhoea (the last being normally very common in Aden).

Examination of the chest revealed abnormality in 1 case only—a pleural rub lasting for 8 days. Tenderness was found in half the cases, mainly subcostal but in 3 cases it was epigastric. Radiographs taken in 25 cases showed the diaphragm to be freely mobile in all. Red-cell counts were normal, but white-cell counts varied from 8,000 to 13,000 per c.mm.; the erythrocyte sedimentation rate was also raised. Twelve out of 30 male patients had orchitis, which was the chief complication, starting after the eighth day and lasting from 2 to 6 days. Treatment was symptomatic; codeine, aspirin, and the barbiturates were useful, although morphine was sometimes necessary to relieve the severe headache.

Sporadic cases of Bornholm disease need to be carefully distinguished from pleurisy, an upper abdominal surgical condition, and early infective hepatitis. Malaria gave rise to occasional difficulties. The causal agent is not known, though evidence points to a virus infection spread by droplets. Thus, Aden is within 24 hours by air from Egypt, which makes the introduction of infection easy, even where the incubation period is short. Moreover, an R.A.F. officer, his wife, and their 2 children all developed the disease within a period of 11 days, and there were several cases among the hospital staff. The authors do not think that infected water, milk, or food could be incriminated, or that insects were likely to have carried the organism. *T. E. C. Early*

2181. **Significance of Simultaneous Alkalosis in Experimental Nephrogenic Osteodystrophy and Lead Osteopathy.** (Die Bedeutung einer gleichzeitig bestehenden Alkalose bei der experimentellen nephrogenen Osteodystrophie und bei der Bleiosteopathie)
A. Berner. *Schweizerische Medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **77**, 352–357, March 22, 1947. 7 figs., 29 refs.

Administration of sodium bicarbonate to mice injected with uranyl nitrate, $UO_2(NO_3)_2$, or thallium sulphate, $TlSO_4$, prevented the development of nephrogenic osteopathy (proliferation of osteoclasts and fibrosis of bone marrow), although it was without effect on the kidney lesions produced by these heavy metallic salts. Sodium bicarbonate did not prevent the development of bone lesions caused by chronic administration of lead chloride. The bone lesions in uranium and thallium poisoning are attributed to acidosis associated with the kidney damage produced by these heavy metals; hence the beneficial effect of bicarbonate. Lead, on the other hand, has a direct effect on bone, and this is not modified by the administration of alkali. *G. Popják*

2182. **Bone Nutrition in Mental Diseases.** (El trofismo óseo en las alienadas)
M. R. Castex, L. Estévez Balado, and D. A. Galzerano. *Prensa Médica Argentina* [*Prensa méd. argent.*] **34**, 1627–1664, Aug. 29, 1947. 16 figs.

Neurology

2183. **Consensual Hypothermia of Limbs in the Normal Subject and in Gunshot Injuries of Nerves.** (Die konsensuelle Hypothermie der Gliedmassen bei Gesunden und Nervenschussverletzten)
K. GOLLWITZER-MEIER. *Deutsche Medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **72**, 103–105, March 14, 1947. 6 refs.

While investigating local carbonic acid baths at the Institute of Experimental Pathology and Balneology, Hamburg University, the author noticed consensual skin temperature changes. Experiments were performed to elucidate consensual vasomotor reactions. Skin temperatures were recorded electrically at corresponding points on the back of both hands of normal subjects, first while a blood-pressure cuff surrounding one upper arm was inflated to 15 mm. below the maximum systolic pressure, and then while the pressure was maintained at 20 mm. above the systolic pressure. Compression was continued for 120 to 180 seconds. Similar investigations were carried out before and after alcohol injection of the stellate ganglion, and on cases of gunshot injuries of nerves with trophic changes and causalgia. The following conclusions were reached: (1) In the normal subject mechanical constriction of the vessels of one arm causes consensual vasoconstriction and hypothermia of the opposite arm. This suggested to the author that the hypothermia of the compressed arm was partly due to increased vasomotor tone. (2) The consensual vasoconstriction and hypothermia is less well marked on the affected side in cases of nerve injury with trophic changes. Injection of the stellate ganglion still further reduces these reflex phenomena. *M. Schieber*

2184. **Mycosis of the Nervous System.** (Micoses do sistema nervoso)
C. DA SILVA LACAZ, J. LAMARTINE DE ASSIS, and J. M. TAQUES BITTENCOURT. *Arquivos de Neuro-Psiquiatria* [*Arch. Neuro-psiquiat.*] **5**, 1–52, March, 1947. 2 figs., 91 refs.

The literature of the neuromycoses is surveyed in detail, and complete reports are given on the authors' 25 cases of paracoccidioidal granulomatosis; only 1 of these had definite neurological manifestations attributable to this infection. Neuromycoses are almost invariably secondary to infections elsewhere, which spread locally or by vascular or lymphatic channels. Some fungi are more neurotropic than others, and this study is chiefly concerned with those found in nervous lesions and with the symptomatology and pathology of such cases. These include infections with trichosporon and candida; torula infections; blastomycosis; coccidioidosis; sporotrichosis; actinomycosis; mucor infections; and Brazilian paracoccidioidosis. The protean symptoms caused by these organisms are shown in abstracts of all the cases found in the extensive bibliography.

Trichosporon and candida infections closely resemble tuberculous meningitis clinically, and the findings in the cerebrospinal fluid do not assist in differentiation, which is rendered more difficult by the close resemblance of the organisms to the cells in the fluid. Complement fixation and intradermal sensitization tests are of some value, but the latter may be positive as a result of a previous mycotic infection. Gentian violet intrathecally and potassium iodide orally, or sodium iodide intrathecally or intravenously, may be given.

Torula infections are the commonest cause of neuromycosis, but cases are often missed or wrongly diagnosed as syphilis or tuberculosis. In 50% of the cases reviewed the infection was localized in the meninges, the changes in the cerebrospinal fluid closely resembling those found with tuberculous infection; the colloidal gold curve was similar to that in neurosyphilis. Cerebrospinal fluid culture was positive in 50% and blood culture in 4%. The relative ease with which the organism can be seen or cultured reduces the value of serological and sensitization tests, but injection of spinal fluid into a rat is of value. There is no specific treatment.

Blastomycosis rarely affects the central nervous system, even when generalized; if it does, infection is either terminal (pyaemia) or the result of direct spread; symptoms are focal or those of toxaemia. Diagnosis depends on culture of the organism or on microscopical examination of the cerebrospinal fluid, though serological and sensitization tests are available. No case with neurological infection has survived.

Coccidioidosis, unlike blastomycosis, has never been transmitted directly from man to man; the possibility of an insect vector is suggested. The commonest neurological form is a leptomeningitis, of which three types exist, two closely resembling a tuberculous infection. In the absence of cutaneous or pulmonary lesions in which the organism can be found, diagnosis depends on culture of the cerebrospinal fluid. Cutaneous sensitization tests are fallible and the blood picture is not specific, nor are serological tests of practical value. The prognosis is grave, for no specific drug is available.

Neurological sporotrichosis is extremely rare. *Sporotrichum schencki* can be cultured with ease on Sabouraud-glucose medium at room temperature, and the Widal-Abrami reaction is positive in a titre of 1 in 800 during the acute stage of the illness. Treatment consists in administration of iodides or gentian violet intrathecally; some sulphonamides have been found effective *in vitro*. Cerebral actinomycosis is also very rare: it has a grave prognosis owing to the formation of multiple abscesses. The infection is usually secondary to a bucco-pharyngeal one and follows an extension to the lungs. The usual symptoms are those of encephalitis; focal signs appear and then those of meningitis. Diagnosis rests on finding the fungus in centrifuged cerebrospinal fluid and culturing it, but biological and biochemical tests may also be

employed. The value of penicillin is still *sub judice*. Three cases of cerebral abscess, all in diabetic subjects, attributed to *Mucor corymbifer* are noted.

Brazilian blastomycosis (*Paracoccidioides brasiliensis*) is a misnomer; the authors prefer the term "paracoccidioidal granulomatosis". It has been intensively investigated in the State of Sao Paulo. Originally an infection of rural workers, it is now invading urban districts and is found in workers in all occupations. Visceral lesions are described; cases with localization in lymphatic tissue are common, but neurological localization is rare—a point of distinction from coccidioidal infections. Repeated examinations of centrifuged and sedimented cerebrospinal fluid are required in order to find the organism and culture it, as well as biochemical and biological tests. Sulphanilamide may be used. Cure is shown by a fall in the erythrocyte sedimentation rate and by clinical improvement. The authors investigated 25 cutaneous and visceral cases for neurological signs and serological changes, and examined the cerebrospinal fluid. They studied complement fixation with blastomycotic and actinomycotic antigens in cerebrospinal fluid and blood, using patients suffering from other infections as controls. Changes in the cerebrospinal fluid were not diagnostic; complement fixation in the cerebrospinal fluid could not be regarded as specific, as a positive result might be secondary to a systemic infection in which the blood–cerebrospinal fluid barrier had allowed the passage of antibodies. In one case the presence of the organism in the nervous system was not established, although there were neurological symptoms and it was found in pharyngeal, laryngeal, and pulmonary lesions; this case responded to treatment with sulphadiazine, of which 4 g. was given daily up to a total of 640 g.

The authors conclude that neuromycotic lesions can be placed in two groups—those in which there is "tumour" formation (abscess, cyst, granuloma) and those in which there is meningitis. Both forms often occur simultaneously. In view of the ambiguity of clinical findings and of findings in the cerebrospinal fluid and blood, diagnosis can rest with certainty only on the actual identification of the organism or culture.

J. J. Keevil

2185. **Hemifacial Spasm. Report of Two Cases**
D. M. GORDON. *Archives of Ophthalmology* [*Arch. Ophthal., Chicago*] **37**, 282–293, March, 1947. 4 figs., 9 refs.

Hemifacial spasm is a condition in which the patient has paroxysms of twitching of the muscles innervated by the seventh cranial nerve of one side. It is not a tic. The orbicularis oculi is frequently the first muscle affected. The spasm, which is usually clonic, may become tonic and persist in sleep. The movement cannot be controlled voluntarily nor can it be reproduced. It does not occur in children, and is worse in the presence of psychic upsets and fatigue. The condition occurs alone or in association with paralysis agitans, encephalitis, disorders of the teeth, neuromata and injuries of the seventh nerve, and conjunctivitis. Cases with a history of injury to the facial nerve have been thought to be due to irregular apposition of the nerve fibres in regeneration, with resulting irregular distribution of seventh-nerve impulses. The most common treatment is surgical division of the facial nerve in whole or in part, or injection of the nerve with alcohol.

A. G. Cross

2186. **The Clinical Picture after Circumscribed Bilateral Degeneration of the Horn of Ammon.** (Über das klinische Bild nach umschriebenem beiderseitigem Ausfall der Ammonshornrinde. Ein Beitrag zur Kenntnis der Funktion des Ammonshorns)
E. GRÜNTHAL. *Monatsschrift für Psychiatrie und Neurologie* [*Mschr. Psychiat. Neurol.*] **113**, 1–16, 1947. 11 figs., 10 refs.

This is a detailed report of a rare and interesting neurological case. The patient, a woman of 67 years, had had mild diabetes for 10 years before being admitted to hospital. A suppurating infection developed on her right foot, necessitating insulin administration and surgical intervention. She was discharged cured and stabilized after 6 months in hospital, but was readmitted after 3 days in hypoglycaemic coma. After the blood-sugar level had been restored the patient exhibited a picture of pronounced dementia. She gave no signs of any intellectual function or of emotional activity. She was continually in a state of unrest, interrupted only by a few hours of sleep. She performed stereotyped circulatory wiping movements with both arms which she ended by putting her fingers into her mouth. In addition she attempted to put everything within her reach into her mouth, and a suck reflex could easily be elicited by touching her cheeks lightly. Corneal reflexes were absent and no pupillary reaction to light was noted, nor did she respond to skin stimuli. She was incontinent and inarticulate. The clinical picture resembled that of a severe and widespread cortical atrophy. At necropsy, however, the only changes found were confined to the horn of Ammon of both hemispheres. In these areas alone there was a complete loss of nerve cells and demyelinization, with proliferation of the neuroglia and development of narrow fissures. Deposits of "pseudo-calcium" were noted in the vessels of that region. [No detailed account of these vascular changes is given.] Everywhere else the brain was normal. The author concludes that the horn of Ammon must be regarded as necessary—together with the cortex—for the development of normal emotions and intellectual functions.

R. Salm

2187. **Contribution to the Study of Spontaneous Subdural Haematomata.** (Contribution à l'étude des hématomes sous-duraux spontanés)
M. FELD. *Revue Neurologique* [*Rev. neurol.*] **79**, 97–108, Feb., 1947. 5 figs.

The existence of non-traumatic subdural haematomata has been questioned, many authors considering that an unnoticed blow is the cause. The present author quotes 5 cases of the traumatic type, in all of which a mild head injury was followed by headaches (sometimes unilateral),

nausea and vomiting, and, in 1 case, by memory changes and depression. Papilloedema was the chief sign; all patients when trephined, usually 2 to 4 months after the injury, were found to have subdural haematomata.

The picture of the non-traumatic type is quite different, a triad of symptoms—namely, headache, wasting, and mental changes—being characteristic. Headache often starts suddenly, is intense and works up to a climax, is unilateral or less commonly widespread, and often paroxysmal. It is made worse by standing and is lessened by lying down; the paroxysms are often accompanied by nausea and vomiting, vertigo, and diplopia or amblyopia. Wasting may be total or may only affect the muscles, often with weakness and difficulty in walking. Less frequently there is difficulty in sleeping, with faults of attention and lessening interest in work; confabulation may be substituted for memory, and the patient may be worried and depressed. It is suggested that lowered intellectual tone (conscience), muscular hypotonus, and wasting are all aspects of the same picture.

Examination reveals papilloedema (73% of cases), tenderness on pressure on the temporal region (also 73%), increased tone in the vertebral muscles, and hyperalgesia. Less commonly found are astasia-abasia, hemiparesis, extensor plantar responses, aphasia, and, occasionally, catalepsy. Direct radiography reveals nothing abnormal, and recourse must be had to ventriculography: anterior-posterior views show distortion of the lateral ventricle on the affected side and displacement towards the midline; in lateral views the ventricles usually appear normal, although one may sometimes seem larger than the other.

Pathological examination reveals the membrane of the haematoma adhering to the dura mater on its parietal surface and covering the cortex on its visceral. If it has existed for some time a capillary bed reinforces the parietal side; sometimes it adheres to the leptomeninges and sometimes is separated by a layer of fluid. The contents consist of greyish-green floccules in dark-brown fluid. The cerebral hemisphere is usually oedematous on the same side and sometimes on the opposite side, and vascular abnormalities are often present. The author suggests that the vascular lesions are secondary.

Six of the author's 15 patients were between the ages of 15 and 30, the remainder being between 45 and 60. The blood pressure was always within normal limits. Several of the patients had suffered from other illnesses; 1 had had pulmonary tuberculosis, another had teeth characteristic of congenital syphilis, 1 was a diabetic, and 1 had jaundice following anthelmintic treatment. The origin remains uncertain, but it does seem certain that spontaneous subarachnoid haemorrhage usually occurs from the rupture of an aneurysm in the circle of Willis or its associated arteries, and on analogy it seems possible that spontaneous subdural haematoma may result from the rupture of varicosities sometimes found in the veins crossing the subdural space. Clearly, however, there is no proof that the haemorrhage is ever "spontaneous", since the memory defects would cover any recollection of slight head injury.

The author believes that in operative technique simple trephining and drainage are not sufficient; the haematoma must be opened (taking care not to damage the adherent external membrane) and its contents evacuated. Fourteen of his patients were operated on; 9 were cured without sequelae, 1 continued to have symptoms, and 4 died (the latter were all above the age of 45). The prognosis is usually good in the young adult, the symptoms and papilloedema disappearing soon after the operation.

T. E. C. Early

2188. **Vascular Changes in Meningitis and their Significance in the Pathogenesis of Cerebral Damage in Early Childhood.** (Gefässveränderungen bei Meningitis und ihre Bedeutung für die Pathogenese frühkindlicher Hirnschäden)

W. J. Eicke. *Virchows Archiv für Pathologische Anatomie und Physiologie* [*Virchows Arch.*] **314**, 88–124, 1947. 8 figs., Bibliography.

The first part of this paper deals with the vascular changes in purulent, tuberculous, syphilitic, rheumatic (allergic), cysticercal, and torular meningitis. The author shows that in acute infections of the meninges, or in the early stages of the chronic infections, the veins are more affected than the arteries. They exhibit polymorphic infiltration of their entire wall, in association with thrombotic processes in their lumina. The tunica media of the larger arteries acts as a barrier to infection for some time, and thus cellular infiltration is at the start confined to the adventitia. The wall of the smaller arteries is infiltrated more rapidly, while the intima may exhibit all changes from swelling and radial arrangement of the nuclei to marked intimal proliferation with thrombosis in the lumen. As a consequence of these vascular changes, degeneration and softening of the neighbouring brain substance occur. If the meningitis heals, all the vascular changes may completely disappear, leaving in some cases only slight thickening of the leptomeninges. The cases which take a subacute course show much of the same features, except that the cellular infiltrate consists of round cells and the veins appear more or less normal. In the chronic infections cellular infiltration is scanty and there may be some fibrous scar tissue in the media, while the intimal proliferation and a fine dust-like fatty degeneration of the intimal cells become very marked. None of these changes in the meningeal vessels is characteristic of a particular disease, but depends solely on the severity and duration of the infection and on the power of the vessels to react to toxic agents. The same exudative, degenerative, and proliferative changes take place in vessels in other parts of the body—for example, in gastric ulcer or ulcus cruris. [In this connexion, it is interesting to note that Cairns and Russell (*J. Path. Bact.*, 1946, **58**, 649) recorded similar findings and arrived at very similar conclusions.]

In the second part of the paper the author records his observations in 50 cases of so-called cerebral infantile paralysis and reports post-meningitic vascular changes in 38. Premature infants who died shortly after delivery and cases of birth trauma are included [this part is less lucid owing to excessive summarizing]. Intrauterine infection of the meninges is mentioned as a cause of congenital vascular lesions. In 12 cases no vascular

abnormalities were observed, though signs of a preceding meningitis were present, such as ependymal granulations, calcareous deposits around the vessels, and fibrosis of the meninges. Thus proliferation of the intima is a frequent, but not a necessary, sequel of meningitis. The author concludes that meningitides of different aetiology are responsible for many cases of cerebral damage in children. *R. Salm*

2189. **Metastases of Uterine Carcinoma to the Central Nervous System. A Clinicopathologic Study**
T. LIPIN and C. DAVIDSON. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat., Chicago*] **57**, 186–198, Feb., 1947. 6 figs., 10 refs.

Metastatic tumours in the central nervous system are usually multiple, but it is possible that carcinomata in some organs may give rise to solitary metastases more frequently than do those in other organs. In a series of 26 cases of uterine carcinoma, 70% gave rise to a single metastasis to the nervous system. Metastases of this origin probably account for 1 to 3% of all carcinomata of the central nervous system. *R. M. Stewart*

2190. **Meningeal Reaction with Abscess of the Brain**
B. J. ALPERS and F. M. FORSTER. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat., Chicago*] **57**, 307–320, March, 1947. 6 figs., 6 refs.

Histopathological studies were made of the meninges in 19 cases with 42 brain abscesses; cases of generalized purulent meningitis were not included. In all but 1 instance evidence of meningitis was observed. The proximity of the abscess to the meninges bore some relation to the degree of meningitis present. There might, however, be an appreciable amount of normal white matter between the focal meningitis and the most external portion of the cavity of the abscess. The meningeal lesion varied from the acute purulent to the chronic adhesive stage, the histological picture changing from that of markedly thickened meninges, infiltrated with polymorphs and heavy deposits of fibrin, to dense fibrous tissue of normal meningeal thickness with only a slight infiltration with lymphocytes. The changes in the meninges adjacent to the abscess were in striking contrast to the state of the meninges elsewhere. In 13 cases the meninges at a distance were normal; in the remaining 6 a moderate number of lymphocytes were present, and in only 3 of these cases were there any polymorphs. The meningitis, even in the acute cases, ceased abruptly where the meninges left the sulcus and passed over the crown of the cerebral or cerebellar convolution. There was also another but less definite limitation of the spread of the inflammation along the length of the sulcus. The stage of inflammation in the meninges could be correlated with the degree of encapsulation of the abscess. In general, the meningeal reaction was more profuse and was of polymorphonuclear type in the acute stages of the abscess, and tended to become less pronounced and lymphocytic in type as the abscess became more chronic and was walled off.

The spinal fluid was available in only 7 cases, but the number and type of cells were fairly accurate indications of the process of encapsulation; thus a mild lymphocytosis indicates a chronic abscess, whereas an increase in polymorphonuclears is associated with an acute abscess which is not yet encapsulated. In some cases, however, the cells were fewer than might be expected owing to the fact that the limiting process in the meninges may seal off the reaction. *N. S. Alcock*

2191. **Serratus Magnus Palsy. With Report of Five Cases**
F. C. ANSANELLI. *Journal of Nervous and Mental Disease* [*J. nerv. ment. Dis.*] **105**, 231–237, March, 1947. 4 refs.

Paralysis of this muscle is not diagnosed as often or as early as it should be. Anatomical and physiological data are given and it is pointed out that the paralysis may be due to trauma or less commonly to infection. Injury to the long thoracic nerve is generally the result of carrying heavy weights on the shoulder or neck or to frequent elevation of the upper limb with over-action of the scalenus medius. Injuries to the shoulder-joint, cervical spine, or supraclavicular region may also damage the nerve. Five illustrative case histories are recorded—3 traumatic and 2 infective in origin.

Winging of the scapula occurs when the arms are pressed forward against resistance. There is also inability to raise the extended arm above the horizontal, with other minor alterations of the relative positions of scapula and spine, and difficulty in such movements as washing the back of the neck and brushing the back hair. The muscle may be involved in toxic neuritis and in traumatic or infectious radiculitis [and in poliomyelitis], but in the latter cases, in contrast to those due to direct trauma to the long thoracic nerve, other sensory and motor symptoms accompany the serratus palsy. The author favours conservative treatment, including the avoidance of difficult movements, application of heat, massage, and passive movements, with the injection of 100 mg. of thiamine chloride daily. In obstinate cases a brace may be valuable; if improvement does not occur in 6 to 12 months, surgical fixation of the scapula to the chest wall will be necessary. *R. G. Gordon*

2192. **Peroneal Palsy Caused by Crossing the Legs**
S. H. NAGLER and L. RANGELL. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **133**, 755–761, March 15, 1947. 7 figs., 16 refs.

The common peroneal nerve is one of the least protected and most vulnerable of the peripheral nerves, and it is particularly liable to injury not only where it runs its independent course but also where it runs side by side with the tibial nerve in the sciatic trunk. It is most likely to be injured where it bends round the neck of the fibula, as it is thinly covered here and both branches are vulnerable to the effects of direct pressure. As the nerve is relatively fixed, flexion of the knee exerts abnormal tension on it, and this movement tends to compress the nerve against the neck of the fibula. Cases

of lesions of the nerve have been reported in trades and occupations which necessitate crouching or kneeling for long periods—for example, miners, agricultural workers, and coal-pickers, and also in bomb-aimers in the air force, who may have to kneel over the bomb-sights for long periods.

The authors report 8 cases of unilateral peroneal palsies in Service personnel, particularly in air-crew technicians. The nerve is liable to be compressed in men who sit with the legs crossed for long periods, but there are frequently other factors present as well, particularly an occupation which involves a crouching position. The body build is a very important factor, and these cases have all occurred in men who are tall, relatively thin, and long-legged. The reason for this is that the nerve is compressed between the head and neck of the fibula of the upper leg and the patella and external condyle of the femur of the lower leg. In short-legged men there may be as much as 6 in. (15 cm.) between these structures when the legs are crossed, so that compression of the nerve does not occur, but in long-legged men the structures frequently come into apposition on crossing the legs, with resulting nerve compression. In 2 of the 8 patients there was muscle weakness but no sensory involvement, due to the fact that the motor fibres are of large diameter and therefore more vulnerable to the ischaemia which results from compression, as demonstrated by Denny-Brown and Brenner (*Arch. Neurol. Psychiat., Chicago*, 1944, **52**, 1). Regarding treatment, the most important factor is prompt recognition and removal of the causal factors, together with mechanical support for the foot, radiant heat, galvanism, and large doses of thiamine. Results of treatment were good.

J. W. Aldren Turner

2193. **Reflex Sympathetic Dystrophy; Report of 57 Cases**

J. A. EVANS. *Annals of Internal Medicine* [*Ann. intern. Med.*] **26**, 417–426, March, 1947. 4 figs., 8 refs.

The complete syndrome of reflex sympathetic dystrophy comprises all the manifestations of sympathetic stimulation—redness or pallor, swelling, sweating, mottled or cystic atrophy of bones, and atrophic changes in muscles and skin as well as the characteristic deep, burning, diffuse pain. There is often a background of vasomotor instability and a hyperemotional temperament or even of hysterical stigmata. Trauma had caused 31 of the 57 cases reviewed. In 36 cases one or more trigger zones were found, injection of which was sometimes followed by disappearance of symptoms, though this was never a satisfactory therapeutic procedure. Diagnosis depends largely on demonstration of relief of pain and other symptoms by sympathetic block with procaine.

In a few cases there was dramatic relief after a single sympathetic block with procaine, but more often there were relapses after a few days or weeks. It is best to resort to sympathectomy in the majority of cases once the efficacy of procaine block has been demonstrated; sympathectomy was carried out on 29 of the 57 patients: 11 obtained complete relief and 11 had 50 to 90% relief for follow-up periods ranging from 1 month to 2 years. Poor results with little or no improvement were obtained in 7 cases, in 2 of which a preliminary diagnostic block had given no relief. In another of the cases of failure a scalenectomy was also considered necessary.

A. M. Stewart-Wallace

2194. **Influence of Menstruation and Geophysical Occurrences on the Frequency of Epileptic Attacks.** (Die Beeinflussung der Häufigkeit epileptischer Anfälle durch Menstruation und geophysikalische Vorgänge. I. Jahresverlauf der Häufigkeitszahlen, Einfluss der Mondphasen und der Menstruation)

R. KLIMMER. *Deutsche Gesundheitswesen* [*Dtsch. GesundhWes.*] **2**, 95–97, Feb. 1, 1947. 1 fig., 5 refs.

The epileptic attacks of 512 patients during 1935 and 1936 were analysed. The incidence was found to be higher during the winter months, but remained uninfluenced by the lunar phases. The ovarian cycle, on the other hand, was shown to exert a decisive influence on the frequency and severity of epileptic attacks. At the beginning of the proliferating stage, at a time when the production of follicle-stimulating hormone is relatively low, severe attacks were commonest. During ovulation (fourteenth to sixteenth day) and the further increase in oestrin production, all forms of attacks were rare. At the end of the secretory phase with the regression of the corpus luteum, few severe attacks, a maximum of slight attacks, and giddiness were noted. All forms of attacks increased during menstruation. From this it would appear that oestrogen therapy might be indicated during the severe post-menstrual attacks and even perhaps later in the cycle. Cases are cited in which there was evidence of endocrine dysfunction in addition to epilepsy and which responded extremely well to hormone therapy.

[Recent work by Markee *et al.* may throw additional light on this subject by its explanation of the oestrogen-adrenaline interrelationship, resulting in occurrence of vascular spasm in the post-menstrual stage and vasodilatation at the time of menstruation.]

H. Jaslowitz

2195. **Epilepsy and Hysteria**

D. N. PARFITT. *Lancet* [*Lancet*] **1**, 483, April 12, 1947. 2 refs.

The author stresses the difficulty of diagnosis between epilepsy and hysteria and also points out that migrainous headaches with vomiting and occasional blackouts may be epileptic in nature. Frank epileptic attacks scarcely need electroencephalography to establish the diagnosis, but in the problem cases, even when the evidence of potential psychological causation may be overwhelming, electroencephalography should, in the author's opinion, be performed, as it may disclose an underlying true epilepsy. Two brief case reports illustrate this, and a third report shows how such cases may be mistaken for migraine. The author notes, as Hurst used to stress in his teaching, that an organic epileptic attack may easily suggest to the patient other attacks which are hysterical.

R. G. Gordon

Psychiatry

2196. **Histological Differential Diagnosis between Alzheimer's Disease and Senile Dementia.** (Diagnostic différential histologique de la maladie d'Alzheimer et de la démence sénile. Pathophobie de la zone de projection corticale)

S. MUTRUX. *Monatsschrift für Psychiatrie und Neurologie* [*Mschr. Psychiat. Neurol.*] **113**, 100–117, 1947. 4 figs., 12 refs.

The histological lesions of Alzheimer's disease and of senile dementia are so similar that qualitative criteria of differentiation appear to be out of the question. Various quantitative criteria have therefore been suggested. These rest on the distribution of the lesions as well as on their numbers. For example, Morel has found that the neurofibrillary changes tend to diminish rapidly on passing from the visual associative centres of the occipital lobe towards the visual receptive area in the calcarine cortex.

The present author has studied the left acousticoreceptive area (Heschl's gyrus and the zones surrounding it). These areas all contain Cajal's " acoustic " type of neurone, found also in the dorsal cochlear nucleus, the inferior corpus quadrigeminum, and the internal geniculate body. Six cases of Alzheimer's disease and 4 cases of senile dementia were studied. All the cases of Alzheimer's disease showed sensory aphasia of varying degree, sometimes with loss of recognition of sounds. This symptom was absent or slight in the control cases. In the former series the dementia began about 10 years earlier, and the age at death was less than in the latter group; the coefficient of Reichardt (difference between brain volume and skull capacity expressed as a percentage of the latter) was, on the average, 18·1% in the former and 13·2% in the latter; Morel's coefficient (capacity of the lateral ventricles expressed as a percentage of the brain weight) was 5·12% in the Alzheimer group and 2·46% in the controls. In both groups arteriosclerosis of the cerebral vessels was present in some brains and had led to localized softenings in 3 cases of senile dementia, but as these lesions appeared to postdate the dementia and did not affect the area examined they were disregarded. In the 4 senile cases the thickness of the cortex was 13·3% less than normal, with no relative paucity of neurones in the third and fifth layers. In the 6 Alzheimer cases the cortex was slightly thicker (10% of normal) but there was relative thinning out of neurones (7·3% in TC, 12·8% in TB, and 15·35% in TA), which was less pronounced in the auditory-receptive area than in the surrounding convolutions. The loss of cells was always greater in the third layer.

There was a marked difference between the two groups in the number and distribution of the characteristic Alzheimer lesions. In only 1 of the 4 senile cases were neurofibrillary changes seen, and then only in area TE—that is, the area furthest from the receptor area; whereas all the Alzheimer group showed these lesions in some or all of the areas examined; they were always more numerous in the areas further removed from Heschl's gyrus. The average number per 0·1 c.mm. of tissue was 0·33 in TC, 1·43 in TB, 2·84 in TA, and 3·32 in TE. They were most numerous in the pyramidal layers 3 and 5, less in the granular layers 2 and 4, and least in layers 1 and 6. The number of senile plaques was approximately the same in the two series in the area TE, but was much greater in the Alzheimer series in the areas TA, TB, and TC. There was a greater incidence of plaques on the four outer layers in the senile cases and on the four inner layers in the Alzheimer cases, the third layer being most heavily involved in both groups. Thus the lesions in both series appeared to begin in the third layer in the associative zone and tended to spread to the deeper layers and towards the receptive area, much more in cases of Alzheimer's disease than in those of senile dementia. Neurofibrillary changes were not seen in either series in the largest pyramidal cells or in the acoustic cells of Cajal. *J. G. Greenfield*

2197. **The Phantom Limb**

J. R. EWALT, G. C. RANDALL, and H. MORRIS. *Psychosomatic Medicine* [*Psychosom. Med.*] **9**, 118–123, March–April, 1947. 8 refs.

Out of a series of 2,284 patients who had undergone amputation 100 who were considered to be making a normal adjustment to their disability were selected at random. The following table shows the incidence of phantom sensations and phantom pain and the comparative incidence of psychiatric disorders in those who were referred for psychiatric advice and in the sample group of 100 " normal amputees ".

	No. of Cases	Psychopathy	Psychosis	Phantom Sensation	Phantom Pain
No. referred because of psychopathology	91	91	11	82	3
No. referred because of violating an Army regulation	61	39	0	55	4
No. voluntarily seeking advice	152	112	0	137	0
No. selected at random, considered " normal" ..	100	64	1	95	1

All the patients who complained of phantom pain presented severe psychiatric disorders; on the other hand, the incidence of psychiatric disorders was much higher than the incidence of pain. Phantom sensations occurred in nearly every case studied carefully, and the terms used to describe the sensations—" twitching, burning, pulling, and aching "—did not differ from the terms used by the

patients who complained of pain. The authors conclude that phantom pain occurs in those individuals who are having phantom sensations but who for psychopathological reasons interpret the sensations as being unpleasant and painful. *P. Mallinson*

2198. **Study of the Blood and Cerebrospinal Fluid Cholinesterase in Various Psychiatric Syndromes.** [Étude des cholinesterases du sang et du liquide céphalo-rachidien dans différents syndromes psychiatriques)
B. GLASSON and S. MUTRUX. *Presse Médicale* [*Pr. méd.*] **55**, 230–231, April 5, 1947. 2 figs., 15 refs.

The authors determined the cholinesterase in the blood serum, red corpuscles, and cerebrospinal fluid in 100 psychiatric patients. The diagnoses included mental deficiency, psychopathy, hebephrenia, catatonia, general paresis, senile dementia, and epilepsy. Though they find considerable differences in the average values for the different groups, their significance cannot be assessed, since the number of cases in the individual diagnostic groups is not given. The authors concluded that the variations in the cholinesterase give no information relevant to the pathogenesis of the psychiatric conditions. *E. Guttmann*

2199. **Relation of Mental Imagery to Hallucinations**
P. F. D. SEITZ and H. B. MOLHOLM. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat., Chicago*] **57**, 469–480, April, 1947. 12 refs.

The concept that hallucinations are an exaggeration of mental imagery is still widely held, though it has not been substantiated by experimental investigation. This problem was made the subject of an extensive investigation, in which no direct relation was found between the predominating type of imagery and the modality of hallucinations.

The "concrete imagery test" used consisted of 130 test words and phrases to which the subject responded with his initial mental image. As a control 114 student nurses were tested. Schizophrenic patients were divided into two groups of 20 patients each. One group included schizophrenic patients with definite auditory hallucinations; the other group included schizophrenics considered to be without auditory hallucinations. A further group of 10 patients, who had fully recovered from an alcoholic hallucinosis, was used as a special control group. All 10 patients had had marked auditory hallucinations.

The data presented showed that the mean percentage of auditory imagery for the schizophrenic patients with auditory hallucinations was significantly lower than for the normal subjects; on the other hand, the schizophrenic patients without auditory hallucinations did not differ from the normal subjects in this respect. The data for the patients who had recovered from alcoholic hallucinosis show that the mean percentage of auditory imagery was also lower than that for the normal subjects, but did not differ from that for the schizophrenic patients with auditory hallucinations. Some qualitative observations made during the tests suggested that the patients with auditory hallucinations actually have difficulty in experiencing auditory images.

The authors, commenting on their results, express the view that one of the facts on which auditory hallucinations may depend is a relatively low percentage of auditory imagery. Such deficiency of imagery is a point of vulnerability, and is more a characteristic of the patient than of his mental illness. This new approach to the mechanism of hallucinations will be the subject of a future paper by one of the authors. *A. Limentani*

2200. **Central Angiospastic Retinopathy. A Psychosomatic Study of its Occurrence in Military Personnel**
M. A. ZELIGS. *Psychosomatic Medicine* [*Psychosom. Med.*] **9**, 110–117, March–April, 1947. 4 figs., 20 refs.

When examining U.S. marines recently returned from the Pacific, the author was struck by the high incidence of macular lesions among these men, most of whom complained of disturbed vision. Ophthalmoscopic examination showed changes in the foveal reflex, crater formation and "holes" in the macular area, together with a central scotoma. Four cases are described in which an acute anxiety state occurred during battle stress shortly before the onset of the ocular symptoms, and the author considers that central angiospasm leading to ischaemic retinopathy represents part of the peripheral vascular response to anxiety. It is, he says, comparable with the disturbance of gastric function and of the renal and coronary circulation and "the many vaso-constrictive manifestations of migraine and other forms of peripheral vasoneuropathy". Treatment in an established case should be directed towards reducing the patient's tension, while neurotic or vulnerable individuals who are considered to be candidates for affectively determined angiospasm should be given preventive psychotherapy.

[The relative frequency of angiospastic retinopathy in stable as compared with unstable individuals is not stated.] *P. Mallinson*

2201. **Camptocormia, or the Functional Bent Back**
S. A. SANDLER. *Psychosomatic Medicine* [*Psychosom. Med.*] **9**, 197–204, May–June, 1947. 8 refs.

Camptocormia, in which the trunk is inclined forward, was relatively common in the British Army in the 1914–18 war, has been little seen in civil life, and was encountered again in the 1939–45 war. The present author thought that these patients exhibited unexpected outbursts of aggression and hostility from time to time. He considers that these cases are very difficult to treat. In a study of 19 he found that there was a strong hero worship for the father often alternating with an irritability and hostility against him. Often the father had something wrong with his back. In 3 cases the mother had serious trouble with her back, but in these cases the father had died before the patient was 5, so that the mother played the part of both parents. Sexual difficulties are common and impotence often occurs before the onset of the camptocormia. The author thinks this may indicate a latent homosexual and/or castration fear. It is generally agreed that camptocormia is a true hysterical symptom, and, especially in war, serves remarkably successfully

to get the patient away from the situation which he finds intolerable.

[Sir Arthur Hurst and his team after the 1914–18 war saw many cases of camptocormia and recognized it as a purely hysterical symptom, which was relieved in the majority of cases quickly and easily. Admittedly some patients relapsed but many did not, and it may be that the apparent difficulty encountered by the author of this article was due to his trying to dig too deeply and find factors which were of less significance than he may have thought.] *R. G. Gordon*

2202. Psychological Invalidism in Thyroidectomized Patients

J. RUESCH, C. CHRISTIANSEN, L. C. PATTERSON, S. DEWEES, and A. JACOBSON. *Psychosomatic Medicine* [*Psychosom. Med.*] **9**, 77–89, March–April, 1947. 3 figs., 26 refs.

Personality studies were carried out on 43 patients from the thyroid clinic of the University of California Hospital. The patients were selected so as to furnish a fair sample of the patients attending the clinic. Thus, 35 were women and 8 were men; 32 had toxic and 11 non-toxic goitres; 13 patients were over 30 and 21 over 40 years of age; 23 made a speedy post-operative recovery, while in 20 recovery was delayed. The clinical diagnoses were confirmed by examination of the specimens removed at operation.

The psychiatric examination consisted of five interviews. The first was devoted to childhood, the second to adult adjustment, the third to the circumstances of the onset of the illness, the fourth to the patient's attitude towards physicians and medicine, and the fifth to social and cultural factors. In addition, each patient was given the Wechsler-Bellevue Test and a shortened form of the Minnesota Multiphasic Personality Inventory. The data thus obtained were compared with the statistical norms for the State of California and the United States, and a detailed analysis of the results is presented. Some of the results were as follows:

Features in common with the population at large.—Average duration of marriage; average number of childless individuals; average distribution of occupation; avoidance of accidents, fractures, and venereal disease; avoidance of conduct disorders.

Features similar to the control group of chronic disease and psychological invalidism.—High divorce or separation rate; above average intelligence; high frequency of hospital treatment and operations; marriage at an early age.

Features characteristic of the group.—Age around 40; few bachelors or spinsters; above-average incidence of patients of foreign parentage; low-grade interests; frequent change of religion.

In the Personality Inventory the female patients scored highest on the hysteria scale and the males on the depression scale; the males showed a high incidence of dependence and of feminine identification. The onset of symptoms was associated with inability to adjust to environmental changes, such as addition to or losses from the family. The childhood anamnesis indicated that, relatively speaking, the fathers tended to have been more affectionate and the mothers authoritarian; the patients were, more generally, either the eldest children or at least among the older members of the family, and had had to undertake responsibility prematurely, owing to the frequency of broken homes. Study of the adult personality revealed that secretly these patients wanted success, but their strict conscience and their need for dependence and guidance seemed to prevent them from achieving their goal. Overtly they conformed to the ideals given by society and social class. Socially, the tendency was for these patients to come from the lower middle class. There was a large incidence of " climbers " and " strainers ", while the importance of culture change is suggested by the large proportion of patients who were foreign-born or native-born of foreign parentage. The patients were more critical of doctors than is the average member of the population, but they expected fulfilment by their physician of certain needs—for example, a need for nurture or for authority or for an ideal with which to identify themselves.

Two-thirds of the patients with a normal childhood recovered without complications, while three-quarters of those with hysterical personalities showed delayed recovery. Among the latter group there was a high divorce rate and a greater number of hospital admissions.

The authors conclude that a pre-operative psychiatric interview might help in the assessment of prognosis by finding the anxious, hysterical, or dependent types, while therapeutic interviews before and after operation might improve the chances of recovery in patients with personality disorders. *P. Mallinson*

2203. An Evaluation of Shock Therapy

L. SALZMAN. *American Journal of Psychiatry* [*Amer. J. Psychiat.*] **103**, 669–679, March, 1947. 94 refs.

The author argues that while shock therapy does produce a more rapid remission of psychotic symptoms it materially decreases the time before the onset of relapse and, moreover, may lead to a definite deterioration of the personality. In other words, however beneficial it may be temporarily, it is definitely detrimental in the end. In the 10 years since the introduction of this form of therapy by Sakel many investigations have been made, but it is claimed that all these studies are not critical enough and do not take into consideration possible remote harmful effects or the subsequent history of the patients over a sufficiently long period.

In the author's series of cases 44 schizophrenic patients received shock therapy and 45 did not. Those who received shock therapy were readmitted, on an average, 3·2 years sooner than those who did not. Thirty manic-depressive patients received shock therapy and 33 did not; the former were readmitted, on an average, 2·96 years sooner than the latter. Similar results were obtained in involutional cases. There is no precise information by which the severity of the cases treated by shock therapy can be compared with that of the controls, since there was no close observation of the early histories. Attention is drawn to physical traumata resulting from shock—fractures, dislocations, and, more important, haemorrhages in the central nervous system—but the number of shocks given was often very large (up to 40

or more) and there is no record of the criteria for selection of cases. Electroencephalographic studies may indicate temporary or permanent damage of the brain after shock.

The author discusses the problem of deterioration after shock. This may not show itself to any great extent in the intellectual field, but there may be considerable change in the general personality, though this is difficult to assess owing to lack of reliable standards. [No consideration is given of how far such deterioration may have been due to the original disease.] In the present series psychometric, Rorschach, and electroencephalographic studies were used. No statistical results are offered but, as is shown by 3 illustrative cases, " the most persistent impression obtained is that the shock patients show a picture resembling the post-lobotomy syndrome ". Finally, it was noted that the diagnosis on readmission of such patients had frequently been changed; it is suggested that shock may alter the behaviour pattern of the patients.

[This will prove a very important paper indeed if the author's conclusions can be confirmed; on the face of it, his evidence is impressive, since it comprises observations on 152 readmitted patients at St. Elizabeth's Hospital and a review of no fewer than 94 papers in the literature on the subject of shock therapy. There are, however, certain objections.] *R. G. Gordon*

2204. **Use of *d*-Tubocurarine Chloride and Thiopentone in Electro-convulsion Therapy**

J. A. HOBSON and F. PRESCOTT. *British Medical Journal* [*Brit. med. J.*] **1**, 445–448, April 5, 1947. 2 figs., 21 refs.

d-Tubocurarine chloride and thiopentone were administered to 50 patients undergoing electro-convulsant therapy (E.C.T.) for psychiatric disorders. Included in the series were patients in whom unmodified E.C.T. would have been contraindicated on account of their physical condition. Some of the patients were hypertensive, arteriosclerotic, and senile; 2 had previously sustained fractures; 1 woman was 5 months pregnant. In their early experiments with *d*-tubocurarine in E.C.T. the authors found that all patients complained of a terrifying feeling of suffocation and weakness after an injection of the drug. Thiopentone (" pentothal ") anaesthesia proved to be the most satisfactory method of producing the required amnesia. The drug has also the advantage of reducing the rise in blood pressure and the excitement which follow the shock.

The treatment was given in the morning, no food being allowed at breakfast-time. Patients received their ordinary sedatives the previous night. *d*-Tubocurarine chloride and atropine sulphate mixed in the same syringe were given intravenously, the syringe was disconnected, and without removing the needle an injection of thiopentone was administered immediately afterwards from another syringe. The average dose of *d*-tubocurarine was approximately 2 mg. per stone (0·3 mg. per kilo) of body weight. The dose varied to some extent with age, sex, and musculature. Atropine in a dose of gr. $\frac{1}{100}$ to $\frac{1}{60}$ (0·65 to 1·3 mg.) counteracts the salivation produced by the drug. Not more than 0·3 g. of thiopentone was required unless there was a tendency to bronchospasm and laryngospasm. This was promptly relieved by a second injection of thiopentone or by nitrous oxide and oxygen. Many of the patients were insufflated with oxygen under slight pressure during the period between administration of *d*-tubocurarine and the shock. Blood pressure and pulse rate were taken before and after the convulsion and at intervals of 15 and 30 minutes later. Temperature was taken before, and at half-hourly intervals for 2 hours after, treatment. A mouth gag was used but no other precaution was taken and no mechanical restraint was applied. Three to 5 minutes after curarization the shock was administered. There was a slight jerk, and after a brief latent period there was a modified clonic convulsion. Depression of respiration and apnoea were observed in most patients and slight cyanosis in about a quarter of the treatments given. The mean increase in systolic blood pressure was 6 mm. Hg (standard error $\pm 1{\cdot}7$ mm.). The pulse rate fell after the convulsion and then rose slightly. There were no complications in the series of 300 treatments, and the only unpleasant symptoms were the usual headache and impairment of memory and concentration. The percentage of patients improved or recovered was similar to that obtained with unmodified E.C.T.

Respiratory depression is the chief danger of curare-controlled E.C.T., and the authors give a sound warning against the use of the drug unless the administrator is experienced and has adequate facilities for controlled respiration at his disposal. The authors believe that with the precautions described the treatment is safer than unmodified E.C.T., and they intend to adopt it as a routine procedure. *A. Limentani*

2205. **Behavioral Changes Produced, in Patients Suffering from Chronic Tensional Anxiety States, by Long-continued Adrenalin Administration**

D. E. CAMERON. *Psychiatric Quarterly* [*Psychiat. Quart.*] **21**, 261–273, April, 1947. 3 refs.

In the treatment of anxiety states with adrenaline a method is proposed for diminishing the patient's response to adrenaline. A standard test is made before and during desensitization; 0·01 mg. of adrenaline in 1 ml. of water is injected intravenously during 30 seconds, the pulse is counted between the fourtieth and the sixtieth second, and the blood pressure measurement is completed at the ninetieth second, the procedure being repeated at 10-minute intervals. Desensitization was attempted by administration of 0·01 mg. of adrenaline intravenously four times in 40 minutes or even as frequently as twenty-five times in 4 hours. In some patients the dose was raised over a period of months to 0·09 mg. In others, 0·02 to 0·08 mg. was given by continuous administration over a period of 2 hours twice daily, and a few patients received additional intramuscular injections of 0·5 to 1 mg. over short periods. Treatment was given two or three times a week, for periods of 6 weeks to 2 years, 41 patients suffering from " autonomous " anxiety states being so treated. Only 2, rather unconvincing, case records are given. *Elliott Emanuel*

Infectious Diseases

VIRUS DISEASES

2206. **South African Institute for Medical Research. Annual Report for the Year ended 31st December, 1946.** Johannesburg [*Rep. S. Afr. Inst. med. Res.*], Johannesburg, 1947. 55 pp.

This report includes an account of an investigation into some aspects of the epidemiology of yellow fever. In Northern Bechuanaland 34 species of mosquito, new for the territory, were found. The predominant mosquitoes biting man both in forest fringing swamps and in open country near the swamps were *Taeniorhynchus africanus* and *T. uniformis*. On a 50-foot high platform built in high forest near Kasane *Aëdes* (*Stegomyia*) *luteocephalus* was the only mosquito taken biting man. Among the indigenous population there is a widespread distribution of immune bodies. Sera from monkeys, 17 *Cercopithecus aethiops*, and 1 *Papio ursinus* were negative for yellow fever antibodies. Local transmission of virus is sporadic and is probably due to a slow and irregular infiltration of infection carried by itinerant labourers from the North. In Barotseland, Northern Rhodesia, sera were collected from 14 *Cercopithecus aethiops*, 2 *Papio ursinus*, 1 cane rat, and 6 birds. All the sera from the mammals were negative, but 2 of the bird sera, 1 from a pelican (*Neopilicanus rufescens*) and 1 from an African openbill (*Anastomus lamelligerus*) gave a positive result.

[The question of protective bodies to yellow fever virus in birds requires further study to determine whether or not these are true immune bodies.] *G. M. Findlay*

2207. **The Complement Fixation Test in Yellow Fever Epidemiology. The Use of Globulin Antigen in Immunity Surveys**

A. PERLOWAGORA and T. P. HUGHES. *Journal of Immunology* [*J. Immunol.*] **55**, 103–119, Feb., 1947. 16 refs.

During the course of epidemiological investigations in epidemic and endemic yellow fever areas the authors devised a complement-fixation test involving the use of a new antigen. The antigen is prepared by treating infective mouse brain, desiccated from the frozen state, with ether to render the tissue lipid-free, and then by precipitating the globulin fraction of a saline emulsion of the anhydrous lipid-free brains with saturated ammonium sulphate solution. The washed and dialysed precipitate, restored to its original volume before the ammonium sulphate treatment, constitutes the antigen, which, when preserved with 1 in 10,000 " merthiolate " and stored at 5° C., retains its antigenicity for at least 3 months. Complement is titrated in the presence of antigen, the mixture being incubated for 1 hour at 37° C. before the addition of sensitized cells. The test is similarly performed with 1 to 1·25 units of complement. Higher serum titres are obtained when the incubation period of 1 hour at 37° C. is followed by an overnight period at 4° C. If this procedure is adopted 1·5 to 2 units of complement is employed. Only sera fixing complement in a dilution of 1 in 8 or greater are considered to be positive.

A series of experiments was undertaken to demonstrate the specificity of this test. Of 305 non-immune human sera 2 (0·7%) showed positive titres. Of 265 Wassermann-positive sera 5 (1·9%) fixed complement at a dilution of 1 in 8. Finally, antigens were prepared in a similar manner from the brains of animals infected with St. Louis encephalitis virus, Japanese B encephalitis virus, West Nile virus, and the recently isolated virus of Ilhéus encephalitis. In addition antigen was prepared from the brains of a group of normal mice. The immune yellow fever serum fixed complement in high dilution in the presence of each of three homologous antigens. There was no fixation with any of the heterologous antigens or with the normal brain preparations. Similarly, a Japanese B antiserum gave fixation only with its homologous antigen.

Human sera obtained during the 1944–5 yellow fever epidemic in Brazil were examined from patients recovered from the disease, from persons with latent infection as shown by the presence of neutralizing antibodies, and from vaccinated individuals. In the first group, of 11 sera taken within 10 days of the reported onset of illness, none possessed complement-fixing antibodies, although 6 gave positive neutralization tests. Of 16 sera taken between the eleventh and thirtieth days, 12 (15%) showed the presence of complement-fixing antibodies. Of 21 sera between the thirtieth and one hundred and thirty-eighth days after the onset of illness, 20 contained complement-fixing antibody and 1 was anticomplementary. A rise in titre was demonstrated in 15 out of 16 cases in which more than one sample was examined.

In the second group 498 sera were obtained from non-vaccinated persons believed to have resided continuously in an endemic area. Of these, 310 (62·2%) were negative by the neutralization test and 188 (37·8%) possessed neutralizing antibodies. Of 305 non-immune sera suitable for testing, 2 fixed complement in a dilution greater than 1 in 4, and of 185 immune sera both neutralizing and complement-fixing antibodies were present in 118 (63·7%). In a further survey in a settlement where yellow fever virus had been isolated on four occasions from marmosets, 10 out of 50 sera contained both neutralizing and complement-fixing antibodies, while of 40 non-immune sera 1 gave a positive complement-fixation reaction. In the third group 38 pairs of sera, pre- and post-vaccinational, were all negative for complement-fixing antibodies. Of a further 29 post-vaccinational samples, only 1 possessed complement-fixing antibodies.

The authors conclude that the test devised by them may have a place of importance in the study of yellow fever

epidemiology as providing a means of determining whether yellow fever immunity has been acquired recently through infection or has been of long standing. Work is continuing to establish whether the antibody measured by this test disappears after a relatively short and constant time interval. *A. Henderson-Begg*

2208. **An Animal Reservoir of Yellow Fever in Africa.** (Sur l'existence d'un réservoir de virus amaril animal en Afrique)
C. Durieux, H. Boiron, and R. Koerber. *Bulletin de la Société de Pathologie Exotique* [*Bull. Soc. Path. exot.*] **40**, 111–118, March–April, 1947. 1 fig., 3 refs.

After pointing out that the existence of monkeys with immune bodies to yellow fever had been demonstrated in a wide area in Africa by Findlay *et al.* (*Trans. R. Soc. trop. Med. Hyg.*, 1936, **29**, 419; 1937, **31**, 103) the authors, working in the Pasteur Institute of Dakar, record their results on monkeys. Of 46 monkeys coming from French West Africa only one, a baboon, *Papio papio*, from the French Sudan was positive. In 1944 they obtained 34 monkeys from the north bank of the Gambia River—33 baboons and 1 vervet monkey, *Cercopithecus aethiops sabaeus*; the vervet and 29 of the baboons were positive. Baboons in troops of from 300 to 400 wander about the Gambia; the monkeys were from 1 to 3 years old. *G. M. Findlay*

2209. **Monkeys in Relation to Yellow Fever in Bwamba County, Uganda**
A. J. Haddow, K. C. Smithburn, A. F. Mahaffy, and J. C. Bugher. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. R. Soc. trop. Med. Hyg.*] **40**, 677–700, May, 1947. 3 figs., 15 refs.

The incidence of immunity to yellow fever among 105 monkeys from the Bwamba forest region of Uganda was high among the twelve species and subspecies found in the district, in addition to 2 members of the suborder Lemuroidea, and amounted to 61%. No immune monkeys were found on the slopes of the Ruwenzori Mountains, which lie to the east of the lowland area. It is suggested that the lowland colobus monkey (*Colobus polykomos vellensis*, Matschie) is the main species involved in the monkey-to-monkey yellow-fever cycle of the uninhabited forest areas while *Cercopithecus nictitans mpangae* plays an important part in bringing the virus into contact with man. The incidence of immunity increases with age.

[The first monkeys to be found in Uganda with immune bodies to yellow fever were described in 1937 by Findlay and MacCallum, *Trans. R. Soc. trop. Med. Hyg.*, **31**, 103.] *G. M. Findlay*

2210. **Complications of Mumps**
J. Humphries. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **213**, 354–357, March, 1947. 3 refs.

In a 5-year period 214 patients (132 male, 82 female) suffering from mumps were admitted to the Charity Hospital at New Orleans. This paper records the frequency and variety of complications. The author recognizes that the statistics from this group may be misleading, as many mild cases are not admitted to hospital.

Orchitis developed in 38 of the 132 males (28·8%). Of 66 who were 15 years of age or older, 36 (54·5%) developed orchitis, while of the 66 under 15 years, only 2 (3%) showed this complication. In 6 instances both testes were involved; in the unilateral cases the two testes were affected equally. In 1 patient the orchitis preceded the more classical signs by several days. [There is no record of the later effects of orchitis in these patients.] Meningo-encephalitis was proved to be present by spinal fluid tests in 3 cases, though others exhibited suggestive clinical evidence. On clinical grounds the diagnosis of pancreatitis was made in 3 patients, and of oöphoritis in 2 of the 82 females. Myocarditis in a 6-year-old coloured boy was attributed to mumps on the basis of an abnormal electrocardiogram—"a P–R interval of 0·16 second and a sharply inverted T_4"—which became normal when the mumps subsided. One patient in this series, a 7-year-old white girl, showed oedema of the neck and anterior chest wall; a second case was encountered after this series had been analysed.

Of the 82 females, 14 were pregnant. Six had mumps near or at the time of an uncomplicated delivery and the child appeared normal. Three had mumps and toxaemia of pregnancy at the time of delivery; the child was healthy and the neonatal period uneventful. In 1 the onset of toxaemia coincided with the appearance of the parotitis. In 2 patients labour began prematurely, at 7 and 8 months respectively, 2 days after mumps appeared; in both, delivery and puerperium were normal but the babies died. The first weighed 3 lb. 11 oz. (1·7 kg.) and died 1 day after birth; necropsy revealed bilateral pulmonary atelectasis. The second weighed 4 lb. 11 oz. (2·2 kg.) and lived for 21 days; no necropsy was performed. Of the remaining 3 patients, 1 was delivered of a normal baby at term, after having made an uneventful recovery from mumps in the seventh month; the child was healthy 5 years later. The second aborted in the fourth month, a week after the onset of mumps. The third had symptoms suggestive of threatened abortion during an attack of mumps in the second trimester. *Henry Cohen*

2211. **Amylase Levels During Mumps. The Findings in Blood and Saliva**
I. J. Wolman, B. Evans, S. Lasker, and K. Jaegge. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **213**, 477–481, April, 1947. 2 figs., 11 refs.

This is a series of 702 careful observations upon the serum amylase in 101 adult males with mumps. The serum level was found to be nearly always elevated in the first week of the illness with a gradual return to normal in the second or third week. The authors believe that this phenomenon is a valuable diagnostic test in cases of obscure swelling in the parotid and jaw region. They bring forward evidence to show that the increase in serum amylase comes from the inflamed parotids and not from the other salivary glands, pancreas, or gonads.
G. F. Walker

2212. **Studies on Malignant Hepatitis**
G. ALSTED. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **213**, 257–267, March, 1947. 2 figs., 13 refs.

As this study from Copenhagen, Denmark, shows, the great increase in acute hepatitis throughout the world in recent years has been fully shared by Denmark. Over 5,000 cases were reported in 1935, but as many as 18,000 in 1943. Most of the patients did well, but in 1944 and 1945 a number of the cases in the author's clinic ran a serious and protracted course. For some quite unknown reason this serious course was predominant in women over 45, in whom the fatality rate was 50%. In the author's own clinic, out of 136 cases admitted from January, 1944, to March, 1946, there were 27 fatal cases in women and only 3 in men. This observation, the author states, is not confined to Copenhagen but seems to be true for all Denmark. Post-mortem examination showed destruction of liver cells and in the more chronic cases much fibrous scarring of the liver. The aetiology remains obscure, and no attempts at transmission were possible in a disease of such serious prognosis. *J. W. McNee*

2213. **Excretion of Urobilinogen in the Urine in Infectious Hepatitis. Serial Studies**
H. A. LINDBERG and G. V. LEROY. *Archives of Internal Medicine* [*Arch. intern. Med.*] **80**, 175–184, Aug., 1947. 5 figs., 5 refs.

POLIOMYELITIS

2214. **The Heart in Acute Anterior Poliomyelitis**
W. I. GEFTER, W. G. LEAMAN, P. F. LUCCHESI, I. E. MAHER, and M. DWORIN. *American Heart Journal* [*Amer. Heart J.*] **33**, 228–239, Feb., 1947. 10 figs., 6 refs.

Following reports in the literature of the post-mortem finding of myocarditis in fatal cases of anterior poliomyelitis, the authors observed carefully 467 cases of acute poliomyelitis admitted to hospital over a period of 3 years.

Clinical evidence of the occurrence of myocarditis was equivocal and is not stressed by the authors. Electrocardiograms were obtained in 226 cases and were considered abnormal in 32 (14·2%). The presence of such abnormalities was not correlated with either age or sex, but they were found with increasing frequency the greater the severity of the disease, the incidence of abnormal findings being 26·1% in severe cases and 4·1% in the non-paralytic cases. Duration of fever seemed to be associated with an increased incidence of abnormality, 10·8% of those who were afebrile after 7 days showing abnormal tracings, whereas the incidence in those with fever longer than 7 days was 24·1%. The authors gained the impression that abnormalities occur early in the disease, do not increase in frequency as the disease runs its course, and persist for several weeks. The most common abnormality encountered was sinus tachycardia of over 140 per minute and disproportionate to the temperature (4%). Left axis deviation (3·5%), flat, diphasic or inverted T waves (3·5%), and a P–R interval prolonged beyond that expected for the patient's age and heart rate (3·1%) were nearly as common. Other findings included high-peaked P waves (2·7%), right axis deviation (2·2%), and elevation or depression of the RST segment (2·2%). Necropsies performed in 6 of the 11 fatal cases revealed pathological changes in the myocardium in 5 cases.

[In discussing the findings the authors would appear to favour the existence of a " poliomyelitis myocarditis ". However, they conclude that the only legitimate inference to be drawn from the electrocardiographic changes is that a myocardial derangement may exist in the disease. The reader is left wondering to what extent these changes were directly attributable to the virus and how much to associated complications.] *B. McArdle*

2215. **Respirator Treatment of Respiratory Paralysis in Acute Anterior Poliomyelitis.** (Om Respirator-Behandling af Respirationspareser ved Poliomyelitis anterior acuta)
E. M. NIELSEN. *Ugeskrift for Læger* [*Ugeskr. Læg.*] **108**, 1341–1348, Nov. 28, 1946. 5 refs.

Observations were made on 110 patients with respiratory insufficiency, of whom 76 were treated in the Sahlin (Swedish) respirator, which produces rhythmic reductions of pressure over the greater part of the thorax and abdomen, while 34 were not given respirator treatment. The average mortality among the respirator-treated patients was 78%; that among the patients not treated in the respirator 67%. In both groups mortality was highest in the patients with signs of bulbar lesions, and lowest—28% of respirator-treated patients and 40% of patients not receiving this form of treatment—in those showing spinal paralysis without signs of bulbar lesions. Post-mortem emphysema of the upper parts of the lungs and atelectasis of the lower parts were pronounced in the respirator-treated patients but not in the others. It is suggested that respirator treatment leads to accumulation of carbon dioxide in the blood and that the consequent acidosis is a further factor contributing to a fatal outcome. It is concluded that respirator treatment should be confined to patients with purely spinal lesions, that it is contraindicated in cases showing signs of bulbar lesions, and that it should never be used prophylactically.
T. R. Parsons

2216. **Isolation of Poliomyelitis Virus from the Throats of Symptomless Children**
H. A. HOWE and D. BODIAN. *American Journal of Hygiene* [*Amer. J. Hyg.*] **45**, 219–222, March, 1947. 4 refs.

From the Poliomyelitis Research Center, Johns Hopkins University, the authors report observations on the presence of poliomyelitis virus in the throats of individuals known to have had various degrees of contact with proved paralytic cases occurring in Baltimore during the summer of 1944.

The method employed was to rub a cotton swab over the tonsillar area and nasopharynx, place it in 1 ml. of

distilled water, and keep it frozen till required for inoculation. The fluid was then expressed in a syringe, brought to *p*H 6·0, shaken, and allowed to stand for 24 hours in the ice-box with 25% of its volume of pure ether, which slowly evaporates during the process; the resulting bacteriologically sterile specimen was injected into the thalami of a rhesus monkey. In most cases injections were made of pools of two or more swabs after reducing the total volume to 1 ml., the whole pool being used on 1 animal. The authors later discovered objections to this proceeding, and consider that certain swabs may have contained antiviral bodies; negative findings are not stressed. It is now considered to be much better to use only one swab for each monkey.

Summarizing their results the authors state that poliomyelitis virus was isolated from 1 of 3 patients suffering from the disease and from 1 of 6 juvenile contacts but from none of 5 adult familial or 7 juvenile and 6 adult extrafamilial contacts of these cases. Virus was found in the throats of 2 out of 28 healthy children frequenting a neighbouring playground. One year later these children had developed antibodies to the virus isolated from them. *Jos. B. Ellison*

2217. **Analogous Reactions of the Poliomyelitis Virus and Cyanogen Compounds**
R. R. Scobey. *Archives of Pediatrics* [*Arch. Pediat.*] **64**, 132–143, March, 1947. 45 refs.

The author offers further support to his theory that the virus of poliomyelitis may be an endogenous protein produced in the body by cyanides, and that it is an excretion product, since it can be obtained from nasal secretion and faeces, has not been found in blood, lymph, or spinal fluid, and is relatively harmless to experimental animals when ingested.

There is a chemical analogy between poliomyelitis virus and cyanogenic substances. Cyanide and the virus are both destroyed by heat and oxidizing agents. Similar paralysis and identical pathological lesions follow the injection either of poliomyelitis virus or of cyanide into animals. Endocrine imbalance renders experimental animals and human subjects susceptible to poliomyelitis and to cyanide poisoning. The hypothyroid type of individual appears to be most susceptible to poliomyelitis. Desiccated thyroid increases the resistance of white mice to acetonitrile, a substance broken down to hydrocyanic acid in the body, and to poliomyelitis virus. Growth lessens animal resistance to acetonitrile and to poliomyelitis. High external temperatures produce hypothyroidism in animals and lowered resistance to acetonitrile, while poliomyelitis epidemics occur under conditions of high temperature, strong light, and humidity. With much iodine in the thyroid, resistance to acetonitrile is increased. Sandler (*Amer. J. Path.*, 1941, **17**, 67) found a connexion between sugar tolerance and susceptibility to poliomyelitis virus, a high tolerance, which is also found in hypothyroidism, corresponding with high resistance.

Liver damage occurs both in cyanide poisoning and in poliomyelitis. This results in an increase of oestrogen in the blood in cyanide poisoning; an increase might be expected in cases of poliomyelitis. Aycock (*Endocrinology*, 1940, **27**, 49) found that a castrated animal treated with oestrogen is less susceptible to the poliomyelitis virus than the castrated animal not so treated. He also found that there is a higher average excretion of oestrogen in patients after an attack of poliomyelitis. He further observed that this disease tends to attack the obese type of individual.

Draper noted that amongst the parents of children with poliomyelitis there were many mothers who had exophthalmos or thyroid enlargement. Thyroid insufficiency is associated with increased permeability of the blood-cerebrospinal fluid barrier by which toxic agents more readily gain access to the central nervous system. To the author these facts seem to indicate that poliomyelitis is one manifestation of a group of diseases originating from a common cause. Diets which facilitate uptake of iodine by the thyroid increase resistance to acetonitrile. In cyanide poisoning and in poliomyelitis, anoxia, toxaemia, and thyroid dysfunction contribute to the inability to utilize vitamins other than B_1. A sulphur deficiency is present in cyanide poisoning, and probably also in poliomyelitis. The benefit obtained in poliomyelitis from thiamine probably originates from the sulphur in its molecule.

The author has treated poliomyelitis with iodine and (in other cases) with thyroid, in conjunction with other therapeutic measures previously described, with striking results, particularly in 1 case. This was one of several which occurred in a village whose drinking water was found to contain cyanide. *B. S. P. Gurney*

2218. **Does Poliomyelitis Virus Grow in Sewage?** [In English]
C. A. Evans. *Acta Medica Scandinavica* [*Acta med. scand.*] **126**, 541–545, March 3, 1947. 9 refs.

The virus of poliomyelitis has been isolated many times from small samples of flowing sewage. The concentration of virus has on occasion been so high that its actual growth and multiplication in the sewage have been postulated. Kling and his associates, for example, estimated that in a single day 3,000,000 monkey-infecting doses of virus were flowing through the sewers of the Norrmalm area of Stockholm, and they suggested that the virus grew in protozoa and other organisms of sewage. Evans and Osterud were unable to demonstrate such growth, and in this paper Evans surveys the literature and decides that an adequate explanation is to be found in the number of carriers and the degree of contamination of faeces without postulating growth in sewage. He argues that the amount of virus in faeces is sometimes much greater than is customarily believed, and that in one instance as little as 0·01 mg. proved an infecting dose. The amount of sewage commonly used to isolate the virus is 1,200 ml., equivalent to 0·5 to 1·5 g. of faeces. If, as is reported, 1% of the population are faecal carriers of the virus, then they contribute on an average 5 to 15 mg. of faeces to such a sample, and this quantity is an adequate infecting dose. Therefore, argues Evans, faecal pollution is an adequate explanation, although the growth of virus is not disproved. *Maurice Mitman*

RICKETTSIAL INFECTIONS

2219. **Rickettsialpox—A Newly Recognized Rickettsial Disease. V. Recovery of *Rickettsia akari* from a House Mouse (*Mus musculus*)**
R. J. HUEBNER, W. L. JELLISON, and C. ARMSTRONG. *Public Health Reports* [*Pub. Hlth Rep., Wash.*] **62**, 777–780, May 30, 1947. 8 refs.

This paper reports the finding of *Rickettsia akari*, the causal agent of rickettsial pox, in the tissues of a naturally infected house mouse (*Mus musculus*) trapped at the site of an outbreak of the disease, a housing development area in the city of New York where more than 100 cases of rickettsial pox have occurred (Sussman, *N.Y. Med.*, 1946, **2**, 27; Shankman, *N.Y. St. J. Med.*, 1946, **46**, 2156). Immunity of mice from infected houses was demonstrated by direct inoculation and by complement fixation. The mice incidentally were also infected with lymphocytic choriomeningitis. Infestation of house mice with mites, *Allodermanyssus sanguineus* (Hirst), and the ability of *A. sanguineus* to transmit rickettsial pox to experimental animals was demonstrated by Huebner *et al.* (*Publ. Hlth Rep., Wash.*, 1946, **61**, 1677).

G. M. Findlay

See also *Abstracts of World Medicine*, 1947, **2**, 332 and 556.

2220. **On the Electrocardiogram in Typhus Fever.** [In English]
L. NORVIIT. *Acta Medica Scandinavica* [*Acta med. scand.*] **126**, 565–578, March 3, 1947. 4 figs., 47 refs.

2221. **On Auriculoventricular Conduction Disturbances in Typhus Fever.** [In English]
L. NORVIIT. *Acta Medica Scandinavica* [*Acta med. scand.*] **126**, 579–588, March 3, 1947. 1 fig., 27 refs.

In the first of these papers the author discusses the electrocardiographic changes in 36 cases of typhus fever, and in the second he investigates in greater detail 9 cases with disturbances of auriculo-ventricular conduction.

In 36 cases of typhus fever electrocardiograms were taken repeatedly during the course of the disease. Convincing clinical signs of an organic heart affection were absent in all cases; changes in the electrocardiograms occurred in 80%. Low voltages, changes in the form of the T wave, and depression of the ST segment appeared chiefly in the febrile period; prolongation of the auriculo-ventricular conduction time and elevation of the ST segment appeared mostly after the fall of temperature.

In the 9 cases with disturbance of auriculo-ventricular conduction the usual abnormality was a simple prolongation of the P–Q interval. Infrequently a partial block of the Wenckebach type occurred. The prolonged P–Q interval was temporarily shortened, usually to normal, by the injection of atropine (5 cases) and adrenaline (1 case). All electrocardiographic changes disappeared in the course of a few days to a fortnight after the fall of temperature.

Necropsies were performed on the 4 fatal cases. One case with a normal electrocardiogram showed histologically an extensive interstitial myocarditis. Of the 3 with abnormal electrocardiograms, interstitial myocarditis was present to a moderate extent in 1 case, to a mild extent in another, and not at all in the third. Electrocardiographic abnormalities need not, therefore, be based on histologically demonstrable myocarditis; on the other hand, myocarditis may be present with a normal electrocardiogram. The author agrees with those authorities who consider that other factors besides myocarditis contribute to the electrocardiographic abnormalities, and mentions particularly functional and exocardial factors. Furthermore, he draws attention to the view, expressed frequently in the literature, that the circulatory phenomena in typhus fever can be explained by affection of the central nervous system alone. In typhus fever there are clinically and pathologically involvement of the central nervous system, affection of the autonomic nervous system, especially the nerve supply of the heart, and changes in blood chemistry, all of which are known to be capable of causing electrocardiographic changes in patients with normal hearts.

Maurice Mitman

2222. **Serological and Clinical Observations in Cases of Epidemic Typhus in Sweden in 1945.** (Serologiska och kliniska iakttagelser vid fall av epidemisk fläcktyfus i Sverige 1945)
E. HAMMARSTRÖM, H. HELLSTEN, and J. FÅHRAEUS. *Nordisk Medicin* [*Nord. Med.*] **33**, 700–706, March 14, 1947. 5 figs., 13 refs.

Four hundred cases of typhus occurred in refugees from German concentration camps arriving in Sweden in 1945; 104 of these were investigated by the Weil-Felix and rickettsia agglutination methods. Two control groups were also investigated at the same time to determine the limit of agglutinating titre which could be considered normal. The first group consisted of 448 healthy Swedes; the titre of anti-OX19 agglutinins exceeded 1 in 320 only in 0·2%. The second group consisted of 334 refugees in whom no clinical evidence of typhus was present, and who had not had the disease or preventive inoculation previously; the anti-OX19 titre exceeded 1 in 640 in 0·6% only. The normal limits of agglutinin titre were accordingly taken as 1 in 320 for the Weil-Felix reaction; 1 in 5,120 was taken as the upper limit of normal in the rickettsia agglutination test.

In the 104 cases investigated, specific agglutinins were demonstrable with the rickettsia test on the fifth day of the disease on an average, but not until the ninth day with the Weil-Felix test. The actual findings are shown below:

Day of Disease	Percentage Positive	
	Rickettsia Agglutination	Weil-Felix
1–3 ..	50	17
4–6 ..	59	10
7–9 ..	84	40
10–12 ..	100	89

The rickettsia agglutination test therefore seems more reliable as a diagnostic method.

D. J. Bauer

2223. **Use of Dimethylphthalate Impregnated Clothing as Protection Against Scrub Typhus**
L. G. WELT. *American Journal of Tropical Medicine* [*Amer. J. trop. Med.*] **27**, 221–224, March, 1947. 1 fig.

This paper is of considerable interest, since it provides proof of the efficacy of dimethylphthalate in preventing the acquirement of scrub typhus in the field. During August to November, 1944, the equivalent of four and a half infantry battalions operated in a river area on an island in the South Pacific, where scrub typhus was endemic in one area. For the purpose of analysis the troops occupying the district were divided into three units: (1) a unit (one battalion in strength) which used no treated clothing; (2) a unit (one battalion in strength) which had all clothing sprayed with dimethylphthalate; (3) a unit (two and a half battalions in strength) which had all uniforms impregnated with an emulsion of 5% dimethylphthalate. The number of cases of scrub typhus which subsequently developed in these three units is shown in the following table:

Group	Use of Dimethylphthalate	Area of Operation	Duration of Operation	No. of Cases
Battalion 1	Not used	Areas 1 and 2; trails 3, 4, 5, and 6.	7–10 days	45
Battalion 2	Clothes sprayed.	Areas 1 and 2; trails 3, 4, 5, and 6.	7–10 days	16
Battalion 3 and successive troops (2½ battalions).	Clothes impregnated.	Area 1 and a few troops in Area 2.	7–10 days	7

The authors note that no dermatitis resulted from the use of the impregnated clothing. *R. M. Gordon*

2224. **Scrub Typhus as a Study in Ecology**
J. R. AUDY. *Nature* [*Nature, Lond.*] **159**, 295–296, March 1, 1947. 2 refs.

This paper is of importance to research workers on scrub typhus, and also to field workers on other diseases who wish to attack their problems from the oecological standpoint, but it is not of direct interest to those primarily concerned with the medical aspects of the disease. It illustrates the principle that parasites with a restricted distribution may be used for "markers" to indicate the wanderings of their host species. Work of this kind is being carried out to give a more exact understanding of the distribution of scrub typhus, and eventually it is hoped that the oecology of the disease will be fully understood. *Kenneth Mellanby*

2225. **Observations on Tsutsugamushi Disease (Scrub Typhus) in Assam and Burma. The Recovery of Strains of *Rickettsia orientalis***
G. E. DAVIS, R. C. AUSTRIAN, and E. J. BELL. *American Journal of Hygiene* [*Amer. J. Hyg.*] **46**, 268–286, Sept., 1947. 7 refs.

2226. **Scrub Typhus Vaccine. Its Effect on Sixteen Cases Incubating the Disease**
W. T. WALKER. *British Medical Journal* [*Brit. med. J.*] **1**, 484–487, April 12, 1947. 4 figs., 2 refs.

During November, 1945, the peak month of the incidence of scrub typhus in Mandalay, 2,500 troops were inoculated with the scrub typhus vaccine prepared at the Wellcome Veterinary Research Station, Frant, Sussex (Buckland *et al. Lancet*, 1945, **2**, 734). The prophylactic course comprised three 1-ml. doses given at weekly intervals.

This report concerns the immediate effect of the inoculation on the course of the disease in 16 men who were incubating the infection at the time of their prophylactic inoculation. The cases have been arbitrarily classified into four groups according to the number of doses of vaccine administered and the length of the interval between their administration and the development of symptoms. A sample case history is given for each group, and the general clinical features of all cases are set out in tabular form. The accompanying table shows the main features of the cases:

Case No.		Date of Inoculation	Date of Onset	Eschar	Fever (in days)	Agglutination (OX K)	
						14th day	21st day
Group I	1	12*	12*	+	32	320	1,280
	2	12	14	+	34	40	1,280
	3	14	14	+	17	80	320
	4	12	14	+	26	80	1,280
	7	14	16	−	12	160	320
	11	10	10	+	14	80	160
	12	10	8	+	18	160	320
Group II	5	12	16	+	15	80	640
	6	14	19	−	12	1,280	—
	8	14	19	+	17	80	320
	9	10	17	+	16	80	320
	10	10	16	+	13	80	640
Group III	13	14 and 21	21	+	12	80	—
	14	18 and 25	23	+	30	80	—
Group IV	15	6, 13, and 20	22	+	10	80	—
	16	12, 19 and 26,	26	+	9	160	—

* All dates refer to November, 1945.

The 4 patients in Groups III and IV had an exceedingly mild infection, scarcely feeling ill at all, and having no complications. The 5 cases in Group II (one inoculation 3 or more days before the onset of symptoms) were all moderately toxic, but the average length of fever (14·5 days) was rather shorter than that of the entire series of 130 cases (17·4 days). In Group I (patients receiving one inoculation less than 3 days before the onset of symptoms) the illness appeared to be modified by a lengthening of the pyrexial period (average duration 21·5 days) accompanied by a reduction and delay in the onset of toxicity. With the exception of the patient in case 2, who was seriously ill, the characteristic symptoms of the

disease were minimal in all cases and the diminution in toxicity was a pronounced feature.

[This paper, dealing as it does with a very small number of partially immunized individuals, provides no satisfactory evidence of the effect of this vaccine on the incidence, mortality, or severity of scrub typhus.]

A. Henderson-Begg

2227. ***para*-Aminobenzoic Acid Therapy of Rocky Mountain Spotted Fever. Outline of a Comprehensive Plan of Treatment with Report of Five Cases**

S. F. RAVENEL. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **133**, 989–994, April 5, 1947. 8 figs., 15 refs.

The name Rocky Mountain spotted fever requires modification. Since 87% of cases in 1945 were found in Central and Eastern portions of the United States its name is no longer apposite, nor is the virulence of the disease, as judged from 241 cases from the South Atlantic States, very much less in the East than in the West. Early advances in treatment seem to have been restricted by the dictum that parenteral fluid administration was dangerous, because of the striking changes in the patient's vascular system. The average mortality rate was 25%.

In 1944 Harrell *et al.* (*J. Amer. med. Ass.*, **126**, 929), having studied the pathology of Rocky Mountain spotted fever, showed that the widespread vascular lesions and starvation caused a serious loss of tissue fluids and protein, diminution in blood chlorides, elevation of non-protein blood nitrogen, and potential or actual peripheral circulatory collapse. Hence treatment should include adequate plasma and blood transfusions together with replacement of dextrose, salts, vitamins, and amino-acids. The intranuclear location of rickettsiae in this disease necessitates the passage of any therapeutic agent through two cell membranes in order to inactivate the causative organisms. Sulphonamides are useless; they are antagonistic to *para*-aminobenzoic acid. Rickettsiae are reported to be penicillin-sensitive, but so far penicillin has proved ineffective against Rocky Mountain spotted fever.

Experimental and clinical work with *para*-amino-benzoic acid in the treatment of spotted fever dates from 1942. The results in animals and human beings show that this drug is a highly effective therapeutic agent. The author reports 5 cases of Rocky Mountain fever treated successfully with *para*-aminobenzoic acid (PABA). The subjects were white children aged from 3 to 17 years; all gave a history of tick bite, headache, and malaise for several days, with rash and fever. Four were delirious. The clinical picture was similar in all the patients. Physical examination and treatment of one of the patients were as follows:

A delirious, dehydrated boy, 17 years old, had a classical haemorrhagic rash, conjunctivitis, palatal enanthem, and scrotal oedema. Serum protein was 6·6 g. per 100 ml. Adequate oral and intravenous fluids were given, with vitamins B and C intramuscularly; 4 g. of sodium chloride was included in the daily diet. *para*-Aminobenzoic acid, 2·5 g. in 25 ml. of a 5% solution of sodium bicarbonate, was given orally 2-hourly for the first 2 days, at the end of which time the blood concentration of PABA was only 4 mg. per 100 ml. Accordingly, the dosage was increased to 5 g. 2-hourly in 50 ml. of solution. After 24 hours the blood level was 18 mg., and a day later 32 mg. per 100 ml. Temperature dropped sharply on the fifth day and reached normal on the sixth, when the rash faded rapidly and the sensorium cleared overnight, leaving the boy almost well. The Weil-Felix agglutination test with *Proteus* OX19 was positive in a titre of 1 in 2,560 twelve days after admission, and the complement-fixation reaction was positive for Rocky Mountain spotted fever in a dilution of 1 in 256 eight days after admission.

The rapid recovery in this rather severe case and in others is claimed as ample justification for viewing PABA as a great advance in the specific treatment of Rocky Mountain fever. Care must be taken to ensure that the amount of the drug given is sufficient to maintain an adequate blood bacteriostatic dose. Too much PABA, however, may result in acidosis; too little buffer in the form of sodium bicarbonate may have the same result. If administration of PABA is stopped too soon, relapse with heart failure and pneumonia may develop. Some patients may continue to be irrational after becoming afebrile, but the sensorium clears as soon as the drug is stopped.

A comprehensive treatment plan must include: (1) Restoration and maintenance of fluid and electrolyte balance with dextrose and saline or lactate–Ringer solution. (2) Correction of acidosis. (3) Maintenance of protein level with high-protein diet, and plasma, serum albumin, and blood transfusion. (4) Administration of vitamins A, C, D, K, and the B complex (liver failure). (5) Administration of PABA, 0·5 to 1 g. per lb. (0·45 kg.) body weight per diem at 2-hourly intervals in buffered solution; determination of the PABA blood level daily (a desirable blood level is 30 to 60 mg. per 100 ml.; 60 to 80 mg. may be necessary: over 80 mg. is hazardous). (6) Careful observation of the patient for toxic effects—acidosis, leucopenia, abdominal distension, and delirium—and for complications—cardiac failure (digitalis), pneumonia (penicillin usually useless), encephalitis. (7) Adequate laboratory studies. (8) Possibly, use of the soluble salt of PABA for parenteral injection.

Arthur A. Bradley

BACTERIAL INFECTIONS

2228. **The Laboratory Diagnosis of Leprosy**

S. MCDONALD. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. R. Soc. trop. Med.*] **40**, 451–456, March, 1947. 3 figs., 9 refs.

Laboratory methods of confirming a clinical diagnosis of leprosy are briefly reviewed with special reference to skin biopsy and its use in the diagnosis of the disease in soldiers in India. The laboratory methods comprise: (*a*) the examination of skin smears stained by the Ziehl-Neelsen method, which is especially suitable for lepromatous and major tuberculoid forms; (*b*) the lepromin test; (*c*) Wassermann and Kahn tests; (*d*) skin biopsy.

Referring to the statement of Rogers and Muir (*Leprosy*, 2nd ed., 1940, Bristol) that skin biopsy is justified only in cases in which bacteriological examinations are negative and clinical signs are doubtful, the author states that most military lepers fall into this

category and that lepromin is not usually available in military practice. It requires an expert histologist to interpret skin biopsies—tuberculosis of the skin, for example, being difficult to distinguish from leprosy; the author briefly summarizes the differences between these. The technique of skin biopsy is as follows:

A wedge of skin at least $\frac{1}{2} \times \frac{1}{8}$ in. (1·25 × 0·3 cm.) in area and $\frac{3}{16}$ in. (0·45 cm.) in depth is removed under local analgesia, fixed in 10% formol-saline for 12 to 24 hours, and left in 95% alcohol overnight; it is then placed successively in absolute alcohol for 4 hours, chloroform for 4 hours, and a saturated solution of paraffin wax in chloroform overnight, and embedded in paraffin wax (one change) for 8 hours. Sections are stained satisfactorily with Ehrlich's haematoxylin and eosin. and beautifully with Weigert's iron haematoxylin followed by Ponceau 2R-acid fuchsin and the use of light green or very dilute Masson's aniline blue as a counterstain.

Of 174 specimens examined, 80 were positive and 14 doubtful, 6 showed other lesions, and 74 could not be diagnosed. Of the positive cases, 79 were tuberculoid and 1 lepromatous. The author considers that skin biopsy "affords the most rapid confirmatory evidence of the tuberculoid types of leprosy most frequently encountered in military practice in India".

J. F. Corson

2229. **A Study of the Diphtheria Antitoxin Response to Recall Doses of Specific Antigen**

F. O. WISHART and M. R. REID. *Canadian Journal of Public Health* [*Canad. J. publ. Hlth*] **38**, 131–140, March, 1947. 8 refs.

The diphtheria antitoxin response to "recall" doses of diphtheria toxoid was studied in eleven groups, totalling 378 persons, living in an area where the incidence of diphtheria was low and where accidental stimulation was unlikely. The first four groups consisted of school-children 7 to 14 years old immunized 6 years previously with three doses of fluid toxoid. Before the recall dose 32% had less than 0·004 unit of circulating diphtheria antitoxin per ml., and 6% less than 0·001 unit. One group was given the Schick test (0·001 Lf toxin), the second the Schick control (0·02 Lf toxoid), the third both test and control, and the last 4 Lf toxoid, subcutaneously. The results obtained from bleedings 5 weeks and 3 years later showed that the antitoxic responses varied with the number of Lf injected, but not in proportion. Thus those receiving 0·001 Lf toxin showed a rise from a mean of 0·007 unit to a mean of 0·071 unit in 5 weeks, falling to 0·22 unit in 3 years; those receiving 0·02 Lf toxoid showed a rise from a mean of 0·007 to a mean of 0·35 unit, falling in 3 years to 0·041 unit. Results in those injected with toxin and toxoid did not differ much from those with toxoid alone. Those injected with 4 Lf toxoid showed the best response, with a mean rise from 0·007 to 1·7 units in 5 weeks, falling to the very satisfactory figure of 0·49 unit in 3 years.

Groups 5 and 6 were graduate students 25 to 50 years old; some had not had diphtheria and some had been recently immunized. The Schick test quantity of toxin and control quantity of toxoid raised the mean antitoxic value from 0·064 unit to 2·6 in 10 days, despite the fact that 8 persons without previous diphtheria or immunization, possessing less than 0·001 unit of antitoxin per ml., and 17 others with more than this amount failed to respond.

Group 7 consisted of 35 university graduates who had received three doses of toxoid 10 to 18 years previously; 31·4% now had less than 0·001 unit per ml. and a further 14·3% less than 0·004 unit. Four Lf of toxoid raised the mean value of 0·025 unit to 9·8 units in 5 weeks; all were above 0·004 unit. Group 8, containing 51 persons, aged 5 to 22 years, immunized 4 to 12 years previously, behaved in much the same way as group 7.

Group 9 (102 medical students) were given the Schick test and control and 2 Lf toxoid. The mean antitoxic value rose from 0·15 to 2·6 units in 3 weeks and, though it seems clear that a large percentage had had diphtheria, 6 with measurable amounts of antitoxin before immunization failed to respond to it by increase in antitoxin titre. Groups 10 and 11 (school-children 5 to 17 years of age, immunized 1 to 10 years previously) were tested intradermally for sensitivity to toxoid, and the positive reactors given 3 Lf of fluid toxoid; the negative reactors were given alternately 3 or 40 Lf toxoid. Three Lf raised the mean antitoxic level from 0·39 unit to 2·8 units, while 40 Lf raised it from 0·28 unit to 8·6 units. Few severe reactions were observed after 40 Lf toxoid, but it is thought that more might have been encountered if the group had not been screened for sensitivity. Three to 4 Lf of toxoid, repeated at 3- to 4-year intervals, is recommended as the recall dose appropriate to most circumstances.

C. L. Oakley

2230. **Typhoid. Clinical Analysis of Three Hundred and Sixty Cases**

B. M. STUART and R. L. PULLEN. *Archives of Internal Medicine* [*Arch. intern. Med.*] **78**, 629–661, Dec., 1946. 6 figs., 9 refs.

This is a detailed clinical study of 360 cases of typhoid fever seen at a hospital in New Orleans between 1939 and 1944. The following criteria were insisted on in the diagnosis: positive blood culture, significant or rising agglutination titre, stool or urine specimen containing typhoid bacilli, or pathognomonic necropsy findings. Two-thirds of the patients came from rural communities, one-quarter living on the river or along the bayous. Many gave a history of drinking from a well or stream, and 50 had been exposed to cases of typhoid among members of their own family. In 11% there was a sudden onset, usually with a transient rigor. Among the rest malaise, headache, and anorexia were the predominant prodromal symptoms. Nearly half had respiratory symptoms. Less than 5% complained of epistaxis. The skin was usually dry. Rose spots were seen in 42% of white patients but in a much smaller percentage of the negroes; in 33% of the patients two or more crops occurred. Multiple furunculosis was seen in 8 patients, typhoid bacilli being isolated from the lesions in 3. Temperature rose in step-ladder fashion to an average maximum of 104·2° F. (40·1° C.), which was maintained for about 11 days, lysis lasting approximately another 8 days. Relapses were observed in 45 cases and second relapses in a further 5.

Neuro-muscular manifestations were very common. Under this heading are included such symptoms of toxaemia as widespread muscular aches and pains, headache, weakness and apathy, stupor and delirium, insomnia, dizziness, and coma. Meningism was often seen and in 1 case actual typhoid meningitis occurred. Conjunctival injection was seen in only 3 patients. Most of the patients had bronchitis; 75 had epistaxis at some time; 5 developed otitis media, 2 requiring mastoidectomy.

During the first week the pulse was slow in relation to the temperature, averaging 96 with dicrotism in a third, characteristically during the third week. During the second and third weeks there was an increase in pulse rate usually proportional to the degree of fever (average maximum 130). A transient systolic murmur developed in 31%. There was 1 case of endocarditis. Venous thrombosis was recognized only three times, a much smaller incidence than usual. Gastro-intestinal symptoms were noted as follows: abdominal tenderness (principally right lower quadrant), 84%; constipation, 79%; distension, 76%; diarrhoea, 43%; gross haemorrhage, 21%; perforation, 7 cases (5 ileum, 2 appendix); parotitis, 2 cases. Enlargement of the liver was seen in 25%, but jaundice occurred in only 13 cases. Ten patients developed cholecystitis and the 7 survivors of these became carriers; 4 were subjected to cholecystectomy but 2 continued to excrete typhoid bacilli in the stools. The authors consider that no patient should be discharged until 3 stool cultures are negative for typhoid bacilli. Splenomegaly was demonstrated in 64%. Typhoid bacilluria was found in 81 patients, but not one of these became a urinary carrier.

Positive blood culture gave the earliest and most conclusive evidence of typhoid; in only 98 of the 360 patients was there no typhoid bacteriaemia (mainly those admitted after the second week of illness). The Widal reaction was positive in significant titre in only 66%, and hence was considered of limited value. Stool culture was positive in only 87 patients. The blood picture showed an initial leucocytosis during the first 10 days, followed by a progressive leucopenia due to decrease in the polymorphonuclear leucocytes, which reached its maximum severity at the end of the third week. Anaemia developed rapidly in all patients, the red cells reaching their lowest numbers at the end of the third week (average 3,200,000 per c.mm.), and returning to normal by the sixth week.

The average duration of stay in hospital was 40 days, the mean duration of the disease before admission being 10 days. There were 45 relapses (1 fatal) and 46 deaths (mortality rate 12·8%); mortality was directly proportional to age. The causes of death were: toxaemia 11, perforation 5 (despite surgical intervention); haemorrhage 7, myocardial failure with pre-existing heart disease 6; other patients died from diabetes mellitus, myocarditis, sulphathiazole reaction, pyelonephritis, and endocarditis. Prognosis was worse in negroes and in people over 40. Treatment was along the usual symptomatic lines, with a liquid, high-calorie diet with supplementary vitamins. About half the patients received transfusions of citrated whole blood.

[Reimann's success with 3 out of 5 patients receiving streptomycin is mentioned, but no reference is made to combined sulphonamide and penicillin therapy.]

E. G. Sita-Lumsden

2231. **Streptomycin in the Treatment of Experimental Brucellosis of Guinea Pigs**

H. L. GILMAN and W. R. LEGROW. *American Journal of Veterinary Research* [*Amer. J. vet. Res.*] **8**, 192–195, April, 1947. 9 refs.

Streptomycin suspended in distilled water and injected intraperitoneally before or after infection failed to overcome experimental brucellosis produced by subcutaneous injection of 10^6 virulent *Brucella abortus* into guinea-pigs. Some bacteriostatic effect was noted in animals treated for long periods, and it is suggested that if a method of administering the drug allowing of slower absorption (intramuscular or subcutaneous injection) had been used, a better result might have been obtained.

[In the discussion it is stated that the drug was injected subcutaneously.] *C. L. Oakley*

2232. **Antibody Formation in Men Following Injection of Four Type-specific Polysaccharides of Pneumococcus**

M. HEIDELBERGER, C. M. MACLEOD, R. G. HODGES, W. G. BERNHARD, and M. M. DI LAPI. *Journal of Experimental Medicine* [*J. exp. Med.*] **85**, 227–230, March 1, 1947. 3 refs.

After human immunization with the capsular polysaccharides of pneumococcus I, II, V, and VII, MacLeod *et al.* (*J. exp. Med.*, 1945, **82**, 445) reported a reduction in the incidence of pneumonia caused by these types (but not of heterologous type pneumonia), as compared with that occurring in a non-immunized control group. The carrier rate for the homologous types was also lowered as compared with that in controls. The authors now report the antibody content of the sera of a random selection from the individuals so immunized 2 months previously. The results were compared with an analysis of their sera before immunization, while the possible effect on antibody content of exposure to infection during the 2-months interval was assessed by a similar analysis of two samples taken at the same intervals from subjects who had received a saline injection in lieu of the polysaccharide solution. Antibody content is recorded as antibody nitrogen in microgrammes of nitrogen per 4 ml. of serum.

Estimations were made by a modified Folin-Ciocalteau method (Heidelberger and MacPherson, *Science*, 1943, **97**, 405; **98**, 63) on anti-C (antibody to species-specific carbohydrate C), anti- I, II, V, and VII, usually precipitated in that order. Several absorptions were sometimes necessary, especially with C substance (and with polysaccharide VII for post-immunization sera). The antibody content for types I, II, and VII was sufficient to account for the favourable protection results obtained, and resembled that found in an earlier series. The response to polysaccharide V was poor, though it had been adequate in the previous series. The levels of the anti-C were high, but remained relatively constant before

and after the injections. The specific antibodies were generally negative or minimal before immunization, and in the control cases remained so. Anti-VII was an exception, being relatively high in certain cases. Such high initial anti-VII content was not necessarily followed by a maximal response to immunization, and remained relatively constant when observed in control cases.

G. T. L. Archer

2233. **A Case of Melioidosis Presenting as an Abscess in the Neck**

C. R. Peck and T. Zwanenburg. *British Medical Journal* [*Brit. med. J.*] **1**, 337–338, March 15, 1947.

An Indian N.C.O. was admitted to a military hospital in Bangkok in February, 1946, complaining of a swelling in the neck, present for 1 month and increasing in size. A fluctuant swelling about 2½ in. (6·25 cm.) in diameter was found just above the suprasternal notch. There was no pain, tenderness, or erythema over the swelling, no lymph-node enlargement, no fever or other constitutional symptom. A leucocyte count was normal. The patient had been resident in Siam for 6 months; there were no other cases in his unit.

The abscess contained a small amount of tenacious yellowish-brown pus, microscopical examination of which revealed scanty Gram-negative rods about 1 μ long showing some degree of pleomorphism and bipolar staining. On culture the organism displayed the typical morphological, cultural, and biochemical characters of *Pfeifferella whitmori*. Intraperitoneal injection into a guinea-pig produced the typical "Strauss reaction", and the organism was recovered from the heart blood and from lesions in the spleen. By the half-plate, gutter, and agar-plate cup methods the organism was found to be resistant to penicillin in strengths up to 100 units per ml. As the lesion was slow in healing under treatment by general surgical measures and antiseptic dressings, an autogenous vaccine was tried at a strength of 500 millions per c.mm. [? misprint for " per c.cm."]. Initial dose was 0·1 ml. subcutaneously, and subsequent doses were increased by 0·1 ml. every 4 days until a maximum of 1 ml. had been reached; there were no untoward reactions. The lesion began to show signs of accelerated healing after the first three or four doses, and the patient was discharged as recovered within 1 month.

T. D. M. Martin

2234. **Penicillin in the Prophylaxis and Treatment of Tetanus.** (La penicillina nella profilassi e nella cura del tetano)

B. Marini. *Policlinico* [*Policlinico*] **54**, sez. prat., 375–380, April 14, 1947.

Reports on the effect of penicillin in human cases of tetanus have been conflicting. The bacillus has been found sensitive to penicillin *in vitro* and successful prophylactically in experimental inoculation of guinea-pigs and rats. The growth and development of *Clostridium tetani* is favoured by the presence of other organisms —such as staphylococci and streptococci—hence penicillin has been tried on account of its bacteriostatic action and for its effects on these other organisms. Kolmer has reported success in cases where antiserum was not obtainable by local surgical treatment and the use of penicillin in doses of 10,000 units 4-hourly for 4 to 6 days. Buxton and Kurmann, in 1945, reported cures of severe cases with moderate doses of antitoxin and injections of penicillin intramuscularly. Altemeier in the following year denied that penicillin was of any value therapeutically in tetanus. He concluded that if there were complications, such as pneumonia, the penicillin might be beneficial, but that the effect as regards tetanus was nil. It must be remembered that penicillin is bacteriostatic and bactericidal or bacteriolytic, but not antitoxic; hence any effect on the symptoms of tetanus is, at least, problematical.

The author gives notes of 10 cases; the results may be summed up thus. Three uncomplicated cases seemed to benefit, but as the advantage was not striking and antitoxin was given at the same time, it is not possible to say whether the benefit was any greater than if the penicillin had been omitted. In 6 other patients there were pulmonary complications; 4 of these died while 2 recovered. The tetanus was severe in all and the penicillin certainly proved beneficial as regards the lung condition, but there was no obvious effect on the tetanus. In the remaining case a youth aged 18 sustained a compound fracture of the femur. He was given prophylactic doses of antitetanus and antigas-gangrene sera; he also received penicillin intramuscularly, 25.000 units for the first dose followed by 20,000 units every 3 hours; in 18 days he received 3,000,000 units. The temperature fell and the penicillin administration was suspended, but was resumed when the fever returned; in 4 days another 880,000 units were injected and the temperature again fell. Nevertheless, 50 days after the accident symptoms of tetanus appeared; antitoxin was given in large doses, 300,000 units daily (100,000 intraspinally), and the tetanus cleared up. The penicillin, though started immediately and given persistently, did not ward off the tetanus.

H. Harold Scott

TUBERCULOSIS

2235. **Pulmonary Resection in the Treatment of Pulmonary Tuberculosis. Analysis of 88 Patients followed for a Period of Two or Twelve Years after Operation**

R. H. Overholt, N. J. Wilson, J. T. Szypulski, and L. Langer. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **55**, 198–222, March, 1947. 5 refs.

In this important paper the authors analyse the results of 92 pulmonary resections for tuberculosis in 88 patients between 1934 and March, 1944. A further group of 104 patients treated during the past 2 years is reviewed. The groups are divided up according to a number of factors, including the extent of the resection (lobectomy or pneumonectomy). In the first group most of the cases were treated between 1942 and 1944, so that follow-up is short; in the second group results are influenced by the improved techniques now used. Of all patients studied for from 2 to 12 years, 42·4% of those who underwent lobectomy and 48·1% of those with

pneumonectomy are clinically well with negative sputum, 18·2% of the former group and 41·2% of the latter being dead. Of the total, however, 26% were desperately ill before operation. Operative fatality for both lobectomy and pneumonectomy is now approximately 5% if a reasonable risk is present, 43·8% if a desperate risk.

The authors feel that resection is the treatment of choice when the following conditions are present: (1) associated suppuration; (2) unilateral disease failing to respond to adequate thoracoplasty; (3) tuberculoma; (4) extensive basal disease with failure of other methods; (5) active parenchymal disease with bronchial stenosis; (6) progressive unilobar or unilateral disease in the adolescent (where artificial pneumothorax has been impossible or has failed); (7) tension cavities in unilobar or extensive unilateral disease; (8) extensive unilobar disease with dense opacities and little fibrosis and retraction; (9) non-expansible lung after pneumothorax with extensive parenchymal disease and with or without complicating tuberculous bronchitis. Tuberculous bronchitis is an indication for resection rather than otherwise.

Permanent bronchial fistula caused tuberculous empyema in a very few cases. Late deaths were usually due to tuberculous complications, most often to contralateral disease. Pneumonectomy gave more gratifying results than lobectomy. In the latter, ipsilateral exacerbation was more evident as a post-operative complication. [On the other hand, contralateral spread seems to have been rather commoner in the former group, and also a rather imposing list of non-tuberculous causes of fatality is mentioned in connexion with it—though the deaths number only 8 out of a group of 58.] In any case, it is important to evaluate pre-operatively the amount and type of disease in other lobes.

The technique now used and found to reduce complications includes analgesia by paravertebral block, local infiltration with procaine, and adoption of the face-down position of the patient during operation. Thoracoplasty after resection is advocated to prevent either overdistension of remaining lobes (following upper lobectomy) or mediastinal displacement (pneumonectomy). Ulceration of the bronchial stump has occurred both early and late after resection. If found during routine bronchoscopy it is treated by application of 30% silver nitrate. Since it is impossible to excise all tuberculous foci prolonged rest in bed after operation is essential.

J. V. Hurford

2236. **Effect of Streptomycin on Experimental Tuberculosis in Guinea-pigs**

L. DICKINSON. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] **2**, 23–26, March, 1947. 5 refs.

The author describes the effect of streptomycin hydrochloride on the growth *in vitro* of *Mycobacterium tuberculosis* (human strain H.148) and on the progress of infection with this strain in guinea-pigs. The virulence was such that 0·0001 mg. of a 3-week culture on a Löwenstein slope consistently gave rise to progressive and fatal disease within 6 months. In the floating pellicle test, with Douglas's modification of Long's medium, growth of H.148 was inhibited by a concentration of streptomycin of 10 units per ml. and partly inhibited at 1 unit per ml.

With Youmans's submerged culture test and the same medium with 10% ox serum added, the effects varied with the size of the inoculum. A small inoculum (0·005 mg. per 10 ml.) was inhibited by 6·5 units streptomycin per ml.; with an inoculum of 0·5 mg. per 10 ml. no inhibition resulted even from 650 units per ml. Six guinea-pigs were given 0·0005 mg. H.148 intraperitoneally and 4 days later treatment with streptomycin was begun (2,000 units per guinea-pig per day for 8 weeks). Six controls similarly infected were left untreated. At necropsy the control animals had extensive tuberculosis of spleen, liver, and lungs and a large local lesion at the site of injection. None of the treated animals had a local lesion and only 1 had more than scattered tubercles in spleen and lungs. In a second experiment three groups of 12 guinea-pigs were given 0·0001 mg. of H.148 intramuscularly. One group had no treatment; the second group received 10,000 units of streptomycin per pig per day for 14 weeks, starting from the date of infection; the third group received similar treatment for 11 weeks, starting 24 days after infection, when 0·05 ml. of old tuberculin gave a positive tuberculin test. After 14 weeks 9 animals from each group were killed, and a numerical assessment of the macroscopic evidence of disease was carried out by the method of Sher and Kloeck. Six animals of the second group and 2 of the third group has no macroscopic evidence of tuberculosis; in other treated animals there was only slight glandular involvement. All the control animals showed widespread macroscopic disease. All spleens were cultured on Löwenstein medium and portions were also ground-up with Ringer's solution; the resulting supernatant fluid was injected into normal guinea-pigs. The results revealed that virulent and viable bacilli were still present even after 14 weeks' treatment. Three animals from each group were left on test after streptomycin treatment ceased to ascertain whether the disease would flare up. After 2 months all showed macroscopic disease of spleen, lungs, and lymph nodes.

The author concludes that streptomycin exercises a marked suppressive action on experimental tuberculosis in guinea-pigs, but, under the conditions of her experiments, it failed to eliminate the disease from the treated animals.

R. J. Lumsden

2237. **Diasone Therapy in Pulmonary Tuberculosis**

G. D. KETTELKAMP and B. FRIEDMAN. *Diseases of the Chest* [*Dis. Chest*] **13**, 23–32, Jan.–Feb., 1947. 5 figs., 10 refs.

Seventeen patients, the majority with far advanced pulmonary tuberculosis, were treated at the Koch Hospital, Missouri, with "diasone". All the patients had sputum containing tubercle bacilli, and the majority rested in bed throughout the period of treatment. The investigation was not controlled. The drug was given in doses of 0·33 g. three times a day, and toxic reactions were, as a rule, slight, the most important being anaemia. Rather fewer than a third of the cases, after an average period of treatment of 200 days, were considered to have

improved; [but inspection of the case records does not indicate that the improvement was remarkable, nor is evidence presented to suggest that such improvement as occurred was due to diasone]. *W. D. W. Brooks*

2238. **Intestinal Tuberculosis: Some Observations**
R. Y. KEERS. *British Journal of Tuberculosis and Diseases of the Chest* [*Brit. J. Tuberc.*] **41**, 33–37, April, 1947. 6 refs.

Little has been written on intestinal tuberculosis, probably because it is usually discovered in the terminal stages of advanced pulmonary disease, when treatment can be only palliative. The record of the 6 cases given in this article is therefore valuable, particularly as in only 1 case did the lesion progress to a fatal issue. It would appear that intestinal tuberculosis does respond well to treatment by ultraviolet light, intravenous injections of 5 ml. of 20% solution of calcium gluconate, and a low-residue high-protein diet. It is, however, difficult to assess the part played by routine sanatorium treatment, and, as the author points out, the permanency of the result depends upon the effective control of the parent lesion in the lung. This contribution to the literature should stimulate interest in a complication that has so far received insufficient attention from clinicians.
Frederick Heaf

2239. **The Antitubercular Action of 1,1,1-Trichloro-2,2-bis-(*p*-aminophenyl)-ethane**
S. KIRKWOOD and P. H. PHILLIPS. *Journal of the American Chemical Society* [*J. Amer. chem. Soc.*] **69**, 934–936, April, 1947. 11 refs.

Studies on the mechanism of action of D.D.T. suggested that 1,1,1-trichloro-2,2-bis-(*p*-aminophenyl)-ethane and 1,1-dichloro-2,2-bis-(*p*-aminophenyl)-ethylene might have antituberculous properties. Both diamines were synthesized by the methods described. They completely inhibited growth of human-type *Mycobacterium tuberculosis in vitro* at 1 in 100,000 concentration. In preliminary experiments the first compound gave " marked control of experimentally induced tuberculosis in guinea-pigs ". *P. D'Arcy Hart*

HELMINTH INFECTIONS

2240. **The Diagnosis of Schistosomiasis Japonica. V. The Diagnosis of Schistosomiasis Japonica by Means of Intradermal and Serological Tests**
W. H. WRIGHT, J. BOZICEVICH, F. J. BRADY, and P. M. BAUMAN. *American Journal of Hygiene* [*Amer. J. Hyg.*] **45**, 150–163, March, 1947. 28 refs.

An account is given of intradermal, flocculation, and formol-gel tests for schistosomiasis japonica carried out on Leyte Island. Military personnel and civilians suffering from the disease provided the opportunity for these tests.

Intradermal tests with antigen prepared from adult *Schistosoma mansoni* in a dilution of 1 in 1,000 produced no response in Service personnel who had a history of infection of not more than 4 to 5 months' duration, but the same antigen used in 28 chronic cases in civilians produced a positive reaction in 78%. Flocculation tests were carried out on 104 cases infected with *S. japonicum*, as shown by the presence of ova in the stools; there were 83·7% of positive reactions. Of these 104 patients, 75 were military personnel, of whom 77% reacted positively; all of the 29 chronic cases in civilians gave a positive reaction. Positive reactions were obtained in 11 out of 70 cases where schistosomiasis was undiagnosed. Of these, 8 were in military personnel, 7 of whom were suffering from unrelated diseases; in the eighth no disease was apparent. The remaining 3 cases were in civilians from a non-endemic area of Leyte. Positive reaction appeared to bear no direct relation to the period of infection, but a marked association existed between the nature of the reaction to flocculation tests and the severity of the symptoms. The formol-gel test proved negative in 111 military cases, including 58 of proved acute infection, positive in 25 out of 34 chronic cases in civilians, and negative in 27 civilians in whom the diagnosis of schistosomiasis had not been established.

The authors consider that the results justify further experimental work on the value of the flocculation test in early diagnosis of the disease. *O. D. Standen*

2241. **Tests of Liver Function in Schistosomiasis Japonica. With Particular Reference to Antimony Treatment and with Report of Two Autopsies**
S. W. LIPPINCOT, F. K. PADDOCK, M. C. RHEES, W. B. HESSELBROCK, and L. D. ELLERBROOK. *Archives of Internal Medicine* [*Arch. intern. Med.*] **79**, 62–76, Jan., 1947. 8 figs., 12 refs.

An account is given of tests of liver function in a group of 481 patients at Harman General Hospital. All the patients had contracted schistosomiasis japonica on the island of Leyte but had not been repeatedly exposed to cercarial infection. The tests were carried out to discover if any liver dysfunction resulted from mild infection compared with the disturbance associated with cirrhosis of the liver due to repeated infection, and also to assess the toxic effects of treatment with tervalent antimony compounds. During the course of serial tests 2 patients died as a result of external violence and complete necropsies were carried out. In both cases death occurred 7 months after the onset of the disease. A report on each case is included with necropsy findings.

Ova had been demonstrated in the faeces in both cases but had disappeared after treatment. In the first case nodules were found throughout the intestines and the liver; in the second case similar nodules were seen in the liver and heart but not in the intestines. In both cases the nodules were associated with minute abscess-like lesions and pseudotubercles. In neither case were the lesions considered to be sufficient to cause abnormal liver function. Results of the tests made on the other patients are in accord with this opinion.

The tests were the bromsulphalein, galactose tolerance, hippuric acid, icterus index, serum bilirubin, and urine urobilinogen tests. Only two of these revealed abnormal figures of any significance—namely, the bromsulphalein

in 12% of 245 cases and serum bilirubin in 6% of 246 cases tested. The tests were carried out during and after treatment, and it was observed that the abnormal values increased during treatment with tervalent antimony compounds ("fouadin" and antimony and potassium tartrate), were higher where a second course of treatment was administered, and persisted for about 90 days after treatment.

The results of the tests indicate that mild infections with *S. japonicum* do not cause serious liver dysfunction and that the tervalent antimony compounds have a direct or indirect minor action on liver function; the evidence provided is insufficient to show the effect of repeated courses of these drugs. *O. D. Standen*

2242. **Schistosomiasis Japonica with Cerebral Manifestations. Report of Seven Cases**
A. J. B. TILLMAN. *Archives of Internal Medicine* [*Arch. intern. Med.*] **79**, 36–61, Jan., 1947. 4 refs.

Seven cases of schistosomiasis japonica showing unusual complications are described. The disease was contracted by military personnel in Leyte. In all cases observations were carried out in the early phase of the disease, and diagnosis was made in the absence of ova in the stools. In 3 cases ova were found relatively early in the period of observation and specific treatment was instituted. In the remaining 4 cases treatment was begun in the absence of ova in the stool; in 1 of these ova were found for the first time at the end of the course of treatment, but in the other 3 cases they were never demonstrated.

The patients, when admitted to hospital, had fever (4 cases), cough or pains in the chest (5 cases), headache (3), and generalized complaints not uniformly present throughout the group. Eosinophilia was present (from 10 to 60%). Marked cerebral manifestations appeared in all cases between 11 and 28 days after admission to hospital. Detailed case histories are given.

The symptoms encountered may be very easily confused with those of other diseases commonly encountered in the area, but a possible exposure to cercarial-infested water should immediately arouse suspicions of schistosomiasis, even when ova are consistently absent from the stool. When hundreds of cases are seen, the clinical syndrome becomes so clear-cut as to permit diagnosis in the absence of rectal tubercles or ova in the stool. With a background of cercarial infection, schistosomiasis can be suspected in the presence of urticarial eruption (in a previously non-allergic subject), pulmonary symptoms, vague gastro-intestinal aches, a leucocyte count of over 15,000, and eosinophilia either above 40% or rising to that figure.

"Fouadin" and antimony and potassium tartrate were used in treatment. Improvement resulted in all cases, including a reduction in the cerebral manifestations, but no claim is made concerning the efficacy of the methods employed. In 1 case it was known that the parasite had not been eradicated. The possibility that the cerebral defects may persist and that there may be secondary involvement of the central nervous system is discussed as well as the likelihood of other cases arising in the United States because the disease has been asymptomatic, or has not been diagnosed, or not entirely cured by treatment. *O. D. Standen*

2243. **Fuadin Therapy in 150 Cases of Schistosomiasis Mansoni with a Follow-up Study of 70 cases**
R. RODIGUEZ-MOLINA and H. SHWACHMAN. *American Journal of Tropical Medicine* [*Amer. J. trop. Med.*] **27**, 117–127, March, 1947. 13 refs.

"Fouadin" (stibophen) was used for the treatment of 150 native Puerto Rican soldiers infected with *Schistosoma mansoni*. All cases were mild or moderately severe, and 55 of them were asymptomatic. The symptom observed most frequently among the remainder was abdominal pain; blood was present in the stools in 21 cases.

The standard course of 10 intramuscular injections of stibophen was given; 1·5 ml. on the first day, 3·5 ml. on the second, 5 ml. on the third, and thereafter 5 ml. on alternate days to a total of 45 ml. About 20% of patients experienced mild toxic effects, the most frequent being pain in the joints. One patient had a local reaction at the point of injection; another had a severe reaction after a total of 15 ml. of the drug, with sudden abdominal pain, fever, and a leucocyte count of 34,000, 79% being eosinophils. The initial eosinophil count for this patient was 20%. The authors suggest that the reaction may have been caused by absorption of protein from worms killed by the drug.

Results of treatment were assessed by examination of the stools on 5 consecutive days beginning 3 days after the last injection. Of the 150 patients, 114 were freed from ova by a single course, and a further 21 by a second course of treatment. Seventy patients were re-examined from 1 to 24 months after the first course of treatment; 39 were found to have relapsed, although 16 of these had received more than one course of injections.

The authors consider that stibophen is not a very efficient drug for the cure of schistosomiasis. They emphasize the importance of following up cases apparently freed from ova at the close of treatment, because conclusions based upon the early effects of the drug are misleading. *L. G. Goodwin*

2244. **Fomite-borne Ancylostomiasis**
E. H. LOUGHLIN and N. R. STOLL. *American Journal of Hygiene* [*Amer. J. Hyg.*] **45**, 191–203, March, 1947. 1 fig., 17 refs.

An epidemiological and clinical study of 3 isolated cases of fomites-borne ankylostomiasis in U.S. Service personnel on Guam is presented. No evidence of the usual forms of exposure could be found, and attention was directed towards the possibility of an occupational infection. The 3 men were laundry workers whose special work was the handling of soiled bed linen from the military hospital, including that from a number of native children and adults heavily infected with hookworms. Investigation showed that all 3 had experienced reddening and itching of the hands and forearms daily after handling soiled linen; they had also had periods of coughing at night for the first 8 to 10 weeks after starting this work.

This evidence led to experimental investigation of soiled linen from the hospital to determine whether infection could come from fomites.

Experiments were performed on seventeen articles of hospital linen, some obviously soiled and some apparently unsoiled with faeces; fourteen articles were known to have come from hookworm-infected cases. The suspected fomites were cultured for 5 days, the linen being kept moist during that period, and then examined for infective larvae by washing and sedimentation. In three instances where faecal stains or faeces were evident, 23,500, 16,100, and 17,700 infective larvae were obtained respectively. In five out of twelve articles from known infected cases on which no faecal soiling was evident, infective larvae developed in numbers from 1,000 to 23,600. Soiled linen often accumulated in the laundry, and conditions there could account for the linen remaining damp for the necessary period of 5 days.

Confirmation of the suspected mode of infection led the authors to investigate the possibility of auto-infection among the native population; in two sets of fomites collected from native houses small numbers of infective larvae were recovered without culture. Experiments on cotton blankets proved that infective larvae could migrate horizontally for a distance of over 8 in. (20 cm.). The authors couple with this the known ability of hookworm larvae to migrate vertically, in order to show how, in bundles of damp clothes, infectivity could be transferred from one article to others.

The conditions imposed upon the native population of Guam as a result of the forcible re-occupation of the island are considered to have increased the possibility of fomites infection by hookworm, because of the lack of sanitary facilities and waterproof dwellings at this period. These suspicions were further supported by the occurrence of an epidemic of hookworm disease involving babies much too young to have become infected in the normal way. The authors consider it not improbable that fomites-borne ankylostomiasis can contribute to persistent endemic hookworm infection.

O. D. Standen

PROTOZOAL INFECTIONS

2245. **The Value of Plasmoquine as a Gametocide in Sub-tertian Malaria**

G. W. A. Dick and R. V. Bowles. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. R. Soc. trop. Med.*] **40**, 447–450, March, 1947.

These observations were made in British Somaliland from February to May, 1944, on Somalis suffering from subtertian malaria. The incidence of gametocytes was found to be high—49% among 215 cases in adults and 54% in another group of 110 cases in natives of all ages. All patients with malaria were given the following course of medical treatment: for adults, quinine sulphate gr. 10 (0·65 g.) three times a day for 3 days, then "atebrin" (mepacrine) 0·1 g. three times a day for 5 days; for children, quinine sulphate gr. 5 (0·32 g.) three times a day at ages between 6 and 12 years, gr. 5 twice a day at ages 2 to 6 years, and gr. 5 daily at ages 6 months to 2 years; the corresponding doses of mepacrine were 0·05 g. thrice, twice, and once daily respectively. "Plasmoquine" (pamaquin) with sodium citrate was then given to alternate patients whose blood showed gametocytes of *Plasmodium falciparum*; adults received 0·01 g. [three times a day] for 3 days, while children had 0·005 g. thrice, twice, and once daily according to age for 3 days. The object of giving pamaquin in alternate cases among those showing crescents in their blood was to observe its effect on gametocytes after a course of quinine and mepacrine.

Two series of observations were made independently, one by each author, in different parts of the Protectorate; Series I was on 45 Somali soldiers, 24 receiving pamaquin and 21 serving as controls, while Series II was on 41 Somali villagers of all ages and both sexes, 22 receiving pamaquin and 19 being used as controls. Gametocytes were looked for on the eighth day of treatment with quinine and mepacrine or on the following day, and pamaquin was then given. The average number of days of survival of gametocytes after the first dose of pamaquin was given was 3 in Series I as against 6 for controls. In Series II the average survival period after pamaquin was 2 days as against over 11 days in controls.

The authors conclude that pamaquin is an effective gametocide in subtertian malaria when used after routine quinine and mepacrine treatment. They think that pamaquin is valuable in areas where the population can be adequately treated, and especially where populations are at times aggregated at relatively isolated places, such as round water-holes, in villages, in barracks, or in a general hospital. It was not possible to observe whether pamaquin prevented relapses. *J. F. Corson*

2246. **Recent Knowledge about Malaria Vectors in West Africa and their Control**

R. C. M. Thomson. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. R. Soc. trop. Med. Hyg.*] **40**, 511–536, May, 1947. 24 refs.

The observations in this paper are mainly concerned with the coastal regions in British West Africa. In each of the four West African colonies malaria control has pursued a more or less independent course, and each colony presents its own peculiar problems. Throughout West Africa *Anopheles gambiae* and *A. funestus* have been regarded for many years as responsible for malaria transmission. The author has now proved that *A. melas* is a species distinct from *A. gambiae*; this distinction is of more than academic interest, since he has shown that the breeding places of *A. melas* are limited to brackish water and occur mainly in the "orchards" of the black mangrove, *Avicennia*, while the much more widespread red mangrove, *Rhizophora*, is relatively harmless. In the Freetown estuary dense breeding places of *A. melas* are mainly confined to about half a dozen *Avicennia* orchards, the total area of which is not more than two or three hundred acres. These areas of swamp have been reclaimed and the breeding grounds of *A. melas* destroyed. In the Lagos area similar operations have been equally successful. The breeding places of *A. gambiae* present a different and much more varied problem, and the author

considers that " during the last few years there has been an increasing realization that the most rapid and striking reduction in the numbers of *gambiae* can be brought about, not by large and costly drainage schemes, but by the so-called temporary measures, systematic search for and treatment or elimination of the small pools and puddles which form the major breeding places. There are many places where breeding grounds have been greatly reduced or eliminated by well-planned drainage schemes . . . but unless these schemes are coupled with an efficient organization for routine inspection and treatment of casual pools, their good effects may be completely nullified ". The author's observations on the value of D.D.T. as a residual insecticide do not support the commonly accepted view that the treatment of the inner walls and ceilings of village houses will make them lethal to mosquitoes for two, or possibly more, months. When mosquitoes " leave the house at any time between dusk and dawn they are attracted by the faint light coming in at windows from outside. We designed a simple trap based on this attraction to faint light in such a way that all mosquitoes leaving the house were trapped in a small detachable window cage. By this means we were able to show that while a house treated with D.D.T. in kerosene remains free of resting anopheles for weeks afterwards, as early as the fourth day after treatment mosquitoes were entering the hut, feeding on the occupants, and leaving the hut after feeding. Of those mosquitoes escaping . . . there was no appreciable mortality in the following 48 hours. Within a week of treatment large numbers of mosquitoes were feeding in the hut every night, all of them leaving afterwards, so that nothing was found in the hut on the following day. Presumably . . . when blood-fed anopheles want to settle on the walls after feeding, they are irritated by slight contact with the treated surface, and quickly leave the hut before they have absorbed a lethal dose of the insecticide. We could find no evidence that mosquitoes were succumbing to the effects of insecticide inside the hut. In another experiment an isolated village had all the houses treated with D.D.T. in kerosene, but we continued to find blood-fed anopheles in outside resting places beside the village, and among those, mosquitoes with gland infections. This irritant quality of the D.D.T. in kerosene, which prevents it exercising its full lethal action, may possibly be overcome by using D.D.T. in other forms, or it may be influenced by the type of house or wall surface. But at present it may prove a serious obstacle, and there is certainly no cause as yet for undue optimism, in West African conditions at least, about revolutionary results of residual spraying with D.D.T. in kerosene ".

The author is careful to point out that these findings may or may not have a bearing on the use of D.D.T. against mosquitoes in houses in other parts of the world.

R. M. Gordon

2246a. **Physiological Factors which Influence the Infection of *Aedes aegypti* with *Plasmodium gallinaceum***
W. HOVANITZ. *American Journal of Hygiene* [*Amer. J. Hyg.*] **45**, 67–81, Jan., 1947. 1 fig., 13 refs.

2247. **Treatment of *Plasmodium vivax* Malaria of Foreign Origin. A Comparison of Various Drugs**
H. H. GORDON, F. R. DIEUAIDE, A. MARBLE, H. B. CHRISTIANSON, and L. K. DAHL. *Archives of Internal Medicine* [*Arch. intern. Med.*] **79**, 365–380, April, 1947. 2 figs., 18 refs.

These observations formed part of a drug-testing programme of the Board for Coordination of Malarial Studies and were made at the Harmon General Hospital, Longview, Texas, U.S.A. Three synthetic drugs—SN 6911 or 3-methyl 4-[4-diethylamino-*l*-methylbutylamino]-7-chloroquinoline—chloroquine; SN 7618 or 7-chloro-4-(4-diethylamino-*l*-methylbutylamino) quinoline [see *Trop. Dis. Bulletin*, 1946, **34**, 708 and 1011]; and SN 8137 or 4-(3-diethylamino-2-hydroxypropylamino)-7-chloroquinoline—were tested in comparison with quinine sulphate and " quinacrine " (mepacrine) hydrochloride. The patients were 593 white soldiers who had been infected with benign tertian malaria (*Plasmodium vivax*) either in the Pacific Area (486) or in the Mediterranean Area (107) and had had relapses or, in some cases, late primary attacks hitherto suppressed by mepacrine.

The drugs were given by mouth to different groups and subgroups of the patients according to a schedule of dosage prescribed by the above-mentioned Board; in each group or subgroup large " priming " [loading] doses were given on the first day of treatment to get a high plasma concentration, and these were followed by smaller doses for varying periods. There were two different courses of quinine, three of mepacrine hydrochloride, one each of the disulphate and binaphthoate of SN 6911, four of chloroquine, and one of SN 8137. Of the 593 patients treated 55 received quinine sulphate, 141 mepacrine hydrochloride, 99 SN 6911, 235 chloroquine, and 63 SN 8137.

This paper records only the clinical results and the microscopical blood examinations, the other laboratory examinations being reserved for separate publication. The results are shown in tables and charts. In assessing the results the authors note various factors which could have influenced them. Parasites disappeared from the blood in 24 hours in 9% of the quinine group, 53% of the mepacrine group, 37% of the SN 6911 group, 66% of the chloroquine group, and 48% of the SN 8137 group; at 48 hours the corresponding figures are 50 [? 59], 95, 92, 98, and 95% respectively. The percentages varied greatly in the subgroups. All the drugs controlled the fever; after 24 to 48 hours the temperature was normal in 70 to 90% of the patients and in all of them after 72 to 96 hours. On the whole there was little difference between the results of different courses of a drug. The newer synthetic drugs caused few minor toxic symptoms; pruritus without rash developed in 17 (7%) of those given chloroquine. These drugs had no advantage over mepacrine, except that they could be used successfully in the rare cases of intolerance to mepacrine; the treatment of such a patient with SN 6911 binaphthoate is recorded.

The patients were observed for 2 to 6 months (mostly 3 to 4 months) after treatment; relapse rates among the Pacific Area groups were high—about 60 to 90%—and

none of the drugs showed any superiority in regard to relapses. The rates varied greatly in the Mediterranean Area groups, but these groups were small, and there were perhaps many strains of parasites and many degrees of infection. Most of the Pacific Area patients relapsed between the fifth and ninth weeks after the end of treatment.

Like mepacrine, the new drugs did not cure but they were effective substitutes for the former in controlling acute attacks and they did not stain the skin. Relapses occurred earlier after SN 6911 than after mepacrine or chloroquine. The possibility of the development of hypersensitivity to these drugs was not investigated.

J. F. Corson

2248. **The Relation to the Course of Avian Malaria of Biotin and a Fat-soluble Material having the Biological Activities of Biotin**
W. TRAGER. *Journal of Experimental Medicine* [*J. exp. Med.*] **85**, 663–683, June, 1947. 6 figs., 34 refs.

2249. **Experimental Chemotherapy of Amebiasis**
H. H. ANDERSON, H. G. JOHNSTONE, and E. L. HANSEN. *American Journal of Tropical Medicine* [*Amer. J. trop. Med.*] **27**, 153–160, March, 1947. 12 refs.

Macaques are suitable monkeys for experimental work on amoebiasis as they are naturally infected with strains of *Entamoeba histolytica* similar to those which infect man; invasion of the tissues occurs and cysts and mobile forms are found in the faeces. The disease in monkeys resembles chronic human amoebiasis.

The authors tested the amoebicidal power *in vitro* for 48 hours at 37° C. of 234 substances, and found that 15 were more active than emetine; 13 of these were tried in 31 naturally infected macaques. The compounds were given orally or parenterally in the maximum tolerated doses daily for periods varying from 5 to 30 days. An electrocardiogram and blood urea and bromsulphalein tests were made before and after treatment. Faecal smears stained with iron-haematoxylin were used for the detection of amoebae; they were examined for 6 successive days at three periods during 3 months: immediately after treatment, 6 weeks later, and after a further 6 weeks.

Eight of the 13 compounds, including emetine hydrochloride, were toxic; of 4 arsenicals the tervalent "carbarsone" oxide (*p*-carbamidophenyl arsine oxide) was the most effective; it was given later by mouth to 5 patients with resistant or chronic amoebiasis, and in 4 the stools were cleared of amoebae during the follow-up period, 6 months in 1 case described; the drug caused no ill effects, but it should be given in enteric-coated tablets to avoid possible irritation of the stomach. Two other tervalent arsenicals which contained sulphur were completely effective in macaques: (1) phenylurea *p*-di-(carboxymethyl)-thioarsenite; (2) 4-carbamido-phenyl-di-(1′-carboxyphenyl-2′-thio)-arsenite. The former has less systemic toxicity than carbarsone oxide; the monkeys showed no amoebae during the follow-up period after seven daily doses of 25 mg. per kilo and there were no ill effects. The latter drug, in the same daily doses for 8 days, was equally effective. Another non-toxic compound, 1-(2′,4′,5′-trimethylbenzyl) 2-aminoethane dihydrochloride, cleared the stools rapidly but only temporarily and was less effective than emetine.

The authors discuss the possible modes of action of various anti-amoebic substances; the antibiotic subtilin was active in tests *in vitro* but enough for *in vivo* tests was not available. It lowers surface tension and causes rupture of the membrane of the amoeba *in vitro*.

J. F. Corson

2250. **Agglutination of *Endamoeba histolytica* Cysts**
R. L. GREIF. *American Journal of Tropical Medicine* [*Amer. J. trop. Med.*] **27**, 131–134, March, 1947. 2 figs., 8 refs.

Cysts of *Entamoeba histolytica* were obtained from cultures of amoeba grown on coagulated egg medium, covered with a modified Locke's solution, for 48 hours. The sediment of the culture was transferred to a tube containing sterile rice starch for 72 hours, then shaken with normal saline and centrifuged at 1,500 revolutions per minute for 5 minutes; this was repeated two or three times. Finally the sediment was shaken with a solution of zinc sulphate and centrifuged, and the supernatant fluid containing cysts and egg particles was drawn off. Three further washings of the sediment got rid of starch and the cysts could be sterilized, if necessary, by washing for 45 minutes in 1 in 50,000 bichloride of mercury followed by further washing with saline.

Agglutination tests were made with the following: (1) fresh sera inactivated at 56° C. for 30 minutes and kept at 4° C.; (2) sera from persons suspected of being infected with *E. histolytica*, preserved with "merthiolate", and stored at 4° C. for several months; (3) biological products from various laboratories, such as concentrated human serum albumin, dried reconstituted normal human plasma, normal horse serum, and normal serum γ-globulin antibodies concentrated fraction II in saline.

The materials were mixed on slides and examined under the microscope; after mixing, the preparations were kept in an incubator at 37° C. for 30 minutes to 2 hours with gentle shaking every 15 minutes; the slides were shaken vigorously just before microscopical examination. Positive and saline controls were used. The results, set out in a table, show that fresh human sera contain certain agglutinins for cysts of *E. histolytica*; agglutination was marked after 2 hours and increased after a further 8 to 10 hours at 4° C. The concentrated γ-globulin fraction II agglutinated the cysts in a dilution of 1 in 400 if kept at 4° C. for 8 hours after the original incubation. Variations in *p*H of the saline diluent between 5·9 and 7·2 did not affect the agglutinins, nor did serum absorption by the bacteria with which the cysts were cultured completely remove the agglutinins. Sterile cysts, as well as those contaminated with bacteria, were agglutinated. One sample showed increased agglutinating power when retested after being kept for 21 days at 4° C. Twenty-nine random samples of fresh serum were tested. but they showed agglutination only occasionally and in low dilution; sterile horse serum, however, agglutinated cysts in dilutions up to 1 in 64. *J. F. Corson*

INFECTIOUS DISEASES OF UNKNOWN ORIGIN

2251. **Atypical Features of Rheumatic Fever in Young Adults**
M. SOKOLOW and A. M. SNELL. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **133**, 981–989, April 5, 1947. 8 figs., 7 refs.

Atypical forms of rheumatic fever are described in which the various major and minor diagnostic criteria laid down by Jones (*J. Amer. med. Ass.*, 1944, **126**, 481) and Griffiths (*ibid.*, 1947, **133**, 974) have not been satisfied. Arthralgia, carditis, fever, and a persistently raised sedimentation rate are the most valuable common criteria for the diagnosis of rheumatic fever in young adults. The other major and minor manifestations are much less common. The articular symptoms may be absent, minimal, mono-articular, fleeting, or intermittent, and the joints of the hands, feet and spine may be affected. The diagnosis of carditis has depended largely on the finding of transient electrocardiographic changes of which partial auriculo-ventricular block and inverted T waves in leads I, II, or IV, alone or in combination, are the most significant. Eight cases are described, and it is suggested that the possibility of rheumatic fever should be considered if fever or arthralgia occurs or if convalescence is protracted in the weeks following a haemolytic streptococcal respiratory infection; appropriate clinical and laboratory investigations should then be carried out. *T. G. Reah*

2252. **The Failure of Massive Salicylate Therapy to Suppress the Inflammatory Reaction in Rheumatic Fever**
T. N. HARRIS. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **213**, 482–487, April, 1947. 2 figs., 27 refs.

Massive salicylate therapy has been very much under examination recently. By this term is meant the giving of between gr. 200 and 300 (13–19·5 g.) of salicylate daily in spite of the well-known toxic effects, such as tinnitus, nausea, and vomiting. Since the work of Coburn it has been widely believed that massive salicylate therapy can suppress the inflammatory reaction in rheumatic fever and prevent cardiac damage. The present authors examined these propositions with special regard to the erythrocyte sedimentation rate and the leucocyte count. They do not seem to have analysed clinical phenomena on the effect on the patient's subjective feelings.

Massive salicylate therapy will certainly lower the erythrocyte sedimentation rate in rheumatic patients. It will do the same in non-rheumatic subjects. On the other hand, massive salicylate therapy does not appear to lower the leucocyte count, and the authors express grave doubt as to the value of the large doses of salicylates now in fashion.

[Only 5 cases were studied in detail and the evidence is not very convincing one way or the other. But Coburn's work (and the clinical trials of those impressed by him) has received something of a challenge.]
G. F. Walker

2253. **Rheumatic Fever. Its Recognition and Treatment**
G. C. GRIFFITH. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **133**, 974–981, April 5, 1947. 31 refs.

Rheumatic fever is defined as a systemic, post-streptococcal, non-suppurative, inflammatory disease with protean manifestations of varying severity and duration in which there is an angiitis due to hypersensitivity manifest in all of the bodily structures. There are four phases of the rheumatic state. The first phase is a haemolytic streptococcal infection of the upper respiratory tract; this is followed by the second phase or period of latency lasting from 1 to 4 weeks. A careful examination at this stage, however, will show that the patient is not symptom-free. The third phase is the period of active rheumatic fever, and the fourth is that of inactivity, which ends only if reactivation occurs.

Four clinical types are recognized: the acute fulminating, the subacute polycyclic, the subacute monocyclic, and the subclinical. The diagnostic criteria are divided into major and minor groups. The major criteria are five in number—namely, a history of a previous attack, carditis, fever, migrating acute arthritis, and chorea. The minor criteria are pneumonitis, tachycardia, subcutaneous nodules, erythemas, epistaxis and purpura, loss of weight, and abdominal pain. Of the major manifestations, carditis is considered to be probably the most important, while fever provides the most frequent evidence of an active rheumatic state. A history of a previous attack is a great help in diagnosis. Formerly, polyarthritis was considered to be the significant sign of the disease, but the articular signs are now considered of less importance. Chorea occurred rarely (0·047%) in this series of patients and was never severe, although other neurological manifestations were observed during the active course of the disease. The disease in its acute form must be differentiated from undulant fever, rheumatoid arthritis, chronic osteoarthritis, tuberculosis, Reiter's syndrome, and the collagenous diseases.

Since there is no specific treatment all available therapeutic agents must be used to prevent death or at least to minimize cardiac damage. Patients suffering from a haemolytic streptococcal infection of the throat should be observed for a longer period than usual and appropriately treated if the active stage of rheumatic fever occurs. Absolute rest in bed, good nursing care, a nutritious diet, and salicylates are the essentials of treatment. Salicylates in the form of sodium salicylate gr. 25 (1·62 g.) and sodium bicarbonate gr. 10 (0·65 g.) every 4 hours or acetylsalicylic acid gr. 20 (1·29 g.) and sodium bicarbonate gr. 20 (1·29 g.) every 4 hours, day and night, with 3,000 ml. of water daily raise the salicylate concentration to the optimum level of 30 to 50 mg. per 100 ml. of blood within 24 to 48 hours. With this dosage unpleasant symptoms are infrequent. The intravenous administration of the drug is rarely necessary. Digitalis is indicated only with the onset of congestive failure, and quinidine is seldom used. Oxygen is of great help in the treatment of rheumatic pneumonitis and congestive failure, and diuretics are only employed

when there is evidence of the latter. Sulphonamides and penicillin are of no value. Only if the diet has been deficient are vitamins added: ascorbic acid has not shortened the duration of the illness; vitamin P has not corrected or prevented the recurrent attacks of petechial haemorrhage; and vitamin K and calcium in large doses have not reduced the increased capillary fragility. Ferrous sulphate gr. 6 (0·39 g.) three times a day is adequate for the correction of anaemia. Fever therapy was not used, but *x*-ray therapy was given in 210 cases in which the disease had been active with one or more recurrences for 6 consecutive months and had not reached the quiescent state on the usual treatment. To 71 patients 100 r was administered through the myocardium weekly for 5 weeks, while the same dosage was given through the myocardium and over the cervical sympathetic ganglia to 63 patients; 67 patients were used as controls. *X*-ray treatment was found to be ineffective. Septic foci should not be removed until at least 6 months after the disease has become quiescent. Blood plasma should not be used, and sera and vaccines were not given.

In the inactive stage a warm, dry climate and regular heliotherapy are of some general benefit. Physiotherapy is harmful in the active stage of rheumatic polyarthritis but is of value in older patients with residual lesions. Patients who have had the disease should be protected against reactivation; if an acute infection of the upper respiratory tract occurs rest in bed is essential, and 300,000 units of penicillin is given daily for 2 or 3 days. Procedures to minimize dissemination of dust have proved beneficial in preventing the spread of respiratory infections. Salicylates do not prevent recurrences nor does the treatment of streptococcal throat infections by sulphonamides and penicillin, but the daily administration of sulphathiazole or sulphadiazine throughout the year will reduce the incidence of such infections by 80%.

Further study of the last measure is necessary to establish its advantages and disadvantages. The use of penicillin pastilles is also now feasible for the prevention of the streptococcal infections. *T. G. Reah*

2254. **Prophylactic Sulphanilamide in Rheumatic Fever: Preliminary Report**
H. L. Stokes. *Proceedings of the Royal Australasian College of Physicians* [*Proc. R. Aust. Coll. Phys.*] **2**, 16–20, Jan., 1947. 1 fig.

The author presents the results to date of sulphanilamide prophylaxis in convalescent and quiescent cases of rheumatic fever. His experience extends over 2 years, during which time sulphanilamide was given to 238 children in doses ranging from 0·5 g. per day to 0·5 g. three times a day. Toxicity was not found to be a serious limiting factor. Close co-operation was maintained with the bacteriological department, and throat swabs and typing were studied in a high proportion of cases. There was no significant decrease in carrier rates of haemolytic streptococci in the treated as opposed to the control group, although there appeared to be a decrease in the number of clinical relapses in the control group. The percentage of organisms resistant to sulphanilamide rose significantly in the treated series, from 7·1 to 31%.

The author comments on these interesting findings, and refers to the experience of American workers in the same field, who found that the induction of drug resistance was a definite danger. It is suggested that prophylactic use of sulphanilamide may be unwarranted, or even dangerous, though as yet there is no proof that the drug-resistant organisms isolated were in fact of the same type as those found in throat swabs before drug therapy.

[The author is continuing this survey; further figures and bacteriology should prove of value.]

D. P. Nicholson

2255. **Treatment of Reiter's Syndrome by Gold Salts**
R. R. Willcox, G. M. Findlay, and A. Henderson-Begg. *British Medical Journal* [*Brit. med. J.*] **1**, 483–484, April 12, 1947. 4 refs.

In animals infection by pleuropneumonia-like organisms is known to cause arthritis and conjunctivitis. Organisms of this group have been isolated from the human genital tract, both in healthy persons and in those suffering from non-specific urethritis. Pleuropneumonia-like organisms are peculiarly sensitive to therapy with gold salts. In view of these facts the authors treated with "myocrisin" 2 patients with Reiter's syndrome.

Cultures of blood and joint fluid for pleuropneumonia-like organisms were negative in both cases. Mice were inoculated with blood and joint fluid in the dorsum of the hind feet. One mouse developed arthritis after 15 days. No definite conclusion should be drawn from this one positive result because mice themselves harbour pleuropneumonia-like organisms capable of causing arthritis. Experience has also shown that members of the pleuropneumonia group are species-specific in their pathogenic action.

The first patient had urethritis, balanitis, and polyarthritis. There was no evidence of gonococcal infection. No improvement was obtained with intravenous injections of T.A.B. vaccine or with sulphathiazole or penicillin therapy. He was given intramuscular injections of myocrisin, from 0·01 to 0·05 g. Over 5 weeks 0·2 g. was given in seven doses. There was slow but marked improvement. All the manifestations of the disease disappeared and the patient was discharged fit for duty. The erythrocyte sedimentation rate fell from 30 to 12 mm. in an hour. The second patient had conjunctivitis in addition to urethritis, balanitis, and arthritis. He was not improved by sulphathiazole or penicillin, and was given a similar course of injections of myocrisin. There was again steady improvement, and the patient was discharged free of symptoms and fit for duty. In neither case did the myocrisin cause a toxic reaction, though a careful watch was kept on the temperature and condition of the skin; the urine was examined daily for albumin while blood counts were made twice weekly.

In view of recent suggestions that Reiter's syndrome is associated with a dysenteric infection, a drop of mixed Flexner vaccine was instilled into the eye of both patients and of a third patient who had apparently recovered from the disease. None of them showed any reaction. Likewise no agglutinins against Shiga's organism were demonstrable in their sera. *D. G. ff. Edward*

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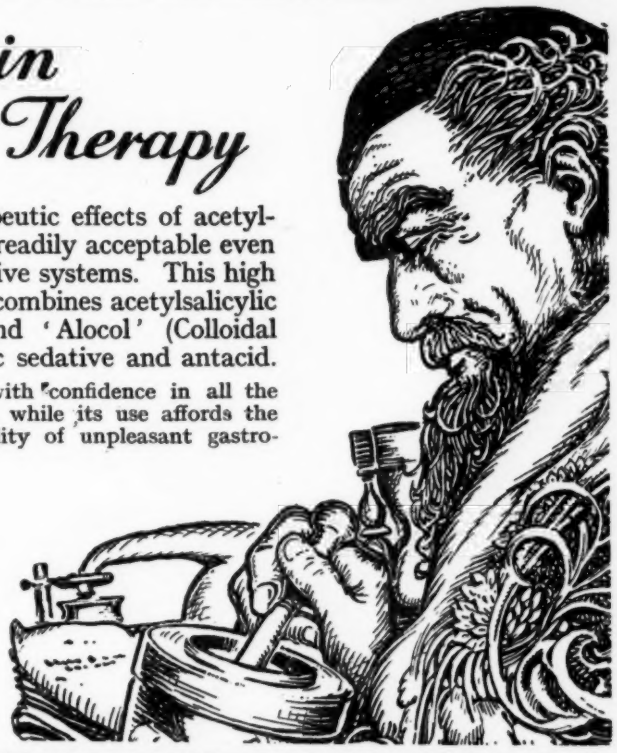

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